SERUM BIOCHEMICAL VALUES IN SICK NEW BORN BABIES

THESIS
FOR
DOCTOR OF MEDICINE
(PAEDIATRICS)

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DINESH KUMAR

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C E R T I F I C A T E

This is to certify that the work entitled "SERUM BIOCHEMICAL VALUES IN SICK NEW BORN BABIES" which is being submitted as a thesis for M.D. (Pediatrics) Examination, 1995 of Bundelkhand University, Jhansi by Dr. Dinesh Kumar, has been carried out in the department of Pediatrics, M.L.B. Medical College, Jhansi.

He has put in the necessary stay in the department as per university regulations.

Dated : 07/1/95

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7/1/95.

(Dinesh Kumar)

C O N T E N T

I N T R O D U C T I O N

While a lot remains undiscovered, mankind with its inquisitiveness has tried to explore and understand the complex mechanisms underlying the basics of life. The study of various biochemical systems has led to the birth of an entirely new discipline of science i.e. Biochemistry.

Like other life forms, human beings also begin life as a single cell. A cell is a complex biochemical entity with molecules of variable size, acting in concordance with each other so as to create a biological system with ability to utilise energy and an inherent capacity to reproduce. The cell functions under influence of chemical messages which are encoded within its nucleus and is transfered at the time of cell division. The cell metabolism and growth is also influenced by various chemical messangers (Harmones) secreted by other cells and transported to it by blood.

Also when the cell is injured it liberates various breakdown products in its mileau, which can be detected in blood by various investigations.

Biochemistry not only helps us to judge the various biochemical reactions underlying the several physiological mechanism of life, but also gives us an insight into the various abberations and deficiencies that may endanger the sustenance of life and produce a diseased state. Thus biochemistry has diagnostic, therapeutic and prophylactice applications.

With the increasing awareness of detrimental effects of various perinatal stresses on the future development of neonate, it has become imperative to employ means and methods, which can ensure early detection of these stressful conditions and thereby reduce perinatal morbidity and mortality. Altered blood chemistry of a neonate can provide early and vital information which may prove helpful in avoiding later complications and sequelae.

Recurrent attacks of hypoglycemia in neonates affects its neurobehavioural development and has been implicated as a cause of mental retardation. Thus simple frequent estimations of blood sugar in critically ill babies can decrease the enormous burden and responsibility which the family and society bears for such mentally deficient persons.

In recent years, there has been increasing recognition of renal failure in the neonatal period, particularly the non oliguric type. Perinatal asphyxia and septicemia are known to cause acute renal failure. Clinical suspicion along with altered blood chemistry (viz. serum creatinine and urea) can prevent many neonates from progressing to complete renal failure.

The present study aims at identifying the alteration in various biochemical parameters in the critically ill neonates.

REVIEW OF LITERATURE

Present century has ushered in an era of great biochemical advances. Strange though it may seem, every disease has now been shown to have some biochemical basis as its cause or effect. Moreover, newborn babies are such a subset of patients who reveal little in terms of sign and symptoms. It is here that biochemical investigations provide an adjunct.

Knowledge of normal level of a given biochemical parameter, and at the same time having some insight into the fluctuation of this value in disease states can help a physician to categorize/stage the patients condition which in turn helps in planning the treatment strategy and predicting the outcome.

However, there are a few studies regarding the various biochemical parameters in sick neonates. Moreover, Indian contributors are disproportionately less and thus the data in our country is very scarce.

The normal biochemical values in neonates have been studied by various Indian workers. Notable contributions have been done by Acharya et al (1965), Walia et al (1981) and Kumar et al (1993).

Very few studies have been carried out in sick neonates. From the times of Von Reuss (1920) and Cornblath (1964) to that of Srinivasan (1986), Heck (1987) and Saili (1991) concepts, methods and techniques have witnessed

dramatic changes e.g. the definition of hypoglycemia has been revised and the entire concept of management of hyperbilirubinemia has undergone revolutionary changes. Again it is well known that with the increasing intensive neonatal care units comming up through out the world, acute renal failure in sick neonates is being increasingly recognised at an earlier stage and as a consequence is better managed.

SERUM SUGAR IN SICK NEONATES

A large number of studies have been conducted in neonates to estimate the incidence of neonatal hypoglycemia. Initial studies were done on whole blood, using non-enzymatic method viz. reduction of alkaline cupric oxide solution to cuprous oxide (Astoor and King, 1954) or of alkaline potassium ferric cyanide to ferrocyanide. However, these values did not represent true blood sugar because of the presence of substances other than glucose in blood which reduced alkaline copper or ferric cyanide solution. The substances include glutathione, uric acid, ascarbic acid, threonine and glucoronic acid.

With the introduction of techniques using glucose oxidase, which oxidises glucose to gluconic acid and has very little effect on any other substances, it is expected that true glucose values are obtained. False et al (1961) reported that uric acid, fluoride, protein precipitants and ascorbic acid could, however, affect the results.

BLOOD/PLASMA /SERUM SUGAR

Whole blood sugar values are 12 to 15 percent lower than plasma or serum sugar. This is due to low water content of red blood cells as compared to plasma.

Whole blood levels are affected by levels of haematocrit. With severe anaemia blood glucose is nearer to serum or plasma levels and vice versa as in polycythemia. According to Zalme and Knowles (1955) for each change of 10 units in haematocrit there is a change in blood glucose by 3-5 mg/dl in the opposite direction. Therefore, there is an increasing emphasis in recent years on using serum or plasma samples.

HYPOGLYCEMIA

There is growing controversy regarding the blood sugar values which should be regarded as hypoglycemia. Cornblath et al (1964) stated that glucose level less than 20 mg/dl in prematures and 30 mg/dl in matures are associated with symptoms of hypoglycemia. This was taken as a standard cut off point for defining hypoglycemia in neonates for many years., until recently when Sexon (1984) Srinivasan (1986), and Heck (1987) proposed that glucose values in the newborn should be maintained at more than 40 mg/dl. This lower limit is clearly higher than that recommended by Cornblath et al (1964, 1973) and Gutberlet and Cornblath (1976).

The new concept is based on the fact that there has been a drastic change in maternal and fetal care with

the administration of glucose containing solutions during labour, delivery and in early days of neonates life that significantly alters the blood glucose concentration.

HYPOGLYCEMIA : CORRENT DEFINITION

Srinivasan et al (1986) defined hypoglycemia as blood sugar concentration that is less than 40 mg/dl between 3 and 24 hours and less than 45 mg/dl after 24 hours of birth. However, Heck and Erenberg (1987) maintained that serum glucose concentration less than 30 mg/dl on first day and 40 mg/dl in the second day of life is hypoglycemic.

CLINICAL FEATURES

Hypoglycemia is an important cause of neonatal morbidity and mortality with long term consequences. Von Creveld (1929) found low levels of total reducing substances in blood of premature infants. Cornblath (1959) reported symptoms associated with low blood sugar lebels in neonates of toxemic mothers. Subsequently Harris and Tizard (1960) described electroencephalographic changes in neonates with convulsions. Zetterson et al (1962) found that in 12 out of 31 newborn infants convulsions were hypoglycemic in origin and responded promptly to glucose administration.

Similar findings of symptomatic hypoglycemia were reported in newborn by Farquhar (1962), Haworth et al (1963), Brown and Wallis (1963).

Neligan et al (1963) attributed hypoglycemia at birth to poor intrauterine nutrition of the fetus. But the authors could not explain why some babies were symptomatic and other were not.

The complex of clinical manifestations that has been attributed to hypoglycemia include episodes of tachypnoea, apnoea, twitching, Jitteriness subnormal temperature, irregular respiration, cyanosis, coma, convulsions, upward rolling of eyeballs, refusal of feeds, sweating and high pitched cry (Cornblath et al, 1967).

A combination of jitteriness convulsions and apneic spells are mot characteristic of hypoglycemia (Cornblath et a., 1967).

HYPOGLYCEMIA AND PREMATURITY

Although level of total reducing substance (Von Crevald, 1929), True sugar (Miller, 1940; Norval, 1950) and glucose has been measured in the blood of premature infants from time to time since 1916, yet there are many conflicting reports in literature regarding the normal level, range and clinical significance of very low values (nearing zero) of blood sugar.

Miller and Ross (1940) found a mean value of 32 mg/dl. Norval (1950) reported a value of 45 mg/dl on first day of life and Ward (1953) observed a mean value of 44.4 mg/dl.

Pincus et al (1956) reported that the concentration of glucose in the plasma was the lowest in very low birth weight babies. The author also found a marked fall in the plasma glucose values determined at the age of four hours and at twenty four hours.

Cornblath et al (1963) in his classical study of blood glucose in premature newborns found that there was a tendency for the level of glucose to be low in the first 3 hours of life. However, the lowest mean level of glucose was present on the third and fourth day of life with subsequent rise over a period of days and weeks. The mean blood glucose varied from 39 to 49 mg/dl in the entire first week of life., although the individual values varied from 15 to 89 mg/dl. Moreover, authors concluded that there was a direct relationship between birth weight and level of glucose in blood and that there was no correlation between glucose and bilirubin levels of blood, as suggested by Ward (1953).

HYPOGLYCEMIA AND I.U.G.R.

Scott, Usher and Mc Lean (1960) reported a high incidence of hypoglycemia and neonatal morbidity in underweight and wasted infants. This has been confirmed in several other studies (Cornblath et al, 1963; Lubchencho et al, 1971) as well.

Intrauterine growth retarded (IUGR) or small for date infants with prematurity constitute the most vulnerable group for developing hypoglycemia.

Neligan (1965) compared prefeeding glucose levels between small for gestational age (SGA) and average for gestational age (AGA) infants . Author found that 12 out of 33 SGA infants had glucose levels below 20 mg/dl. Lubchencho et al (1971) reported that the highest incidence of hypoglycemia occurred in SGA group of infants ($p < 0.001$). Preterm SGA infants had the highest incidence of hypoglycemia (67%), that was significantly higher than found in term SGA and preterm AGA infants ($p < 0.001$). A history of perinatal stress was found in the most of the neonates who developed hypoglycemia. The perinatal stress occurred as a result of complications during pregnancy or labour, resulting in fetal distress and low Apgar score, requiring resuscitation.

SERUM GLUCOSE AND BIRTH ANOXIA

Birth asphyxia is an important cause of neonatal hypoglycemia. Lubchencho et al (1971) found birth anoxia as an important cause of neonatal hypoglycemia in term SGA infants. Harris (1976) in his classical study reported persistent hypoglycemia in term hypoxic infants. Moreover, he observed that the effect of hypoxia was less in preterm AGA and SGA infants. The differences in blood glucose levels between term and preterm infants were significant at 24 and 48 hours of age. Author opined that SGA neonates have more active sympathetic nervous system as a result of prolonged intrauterine 'stress' which

explains higher blood glucose , higher non esterified fatty acid (NEFA) levels and an apparent tolerance to hypoxemia which they have.

SERUM GLUCOSE AND NEONATAL SEPSIS

Young (1970) incriminated the role of neonatal sepsis in causing hypoglycemia. Of the seventeen hypoglycemic neonates studied, eight had hypoglycemic symptoms and nine were asymptomatic. The infecting organisms were chiefly gram negative bacilli. Possible explanations put forth by the author were : inadequate dietary intake during the period of illness, increased metabolic rate resulting in increased utilization of glucose, impaired mobilization of glucose by endotoxins of bacteria.

SERUM SUGAR AND ERYTHROBLASTOSIS - FETALIS

Until recently, hypoglycemia has not been considered a frequent or important complication of erythroblastosis fetalis. Case reportes by Gerrard (1952) Mac Rae et al (1965) described but did not emphasize on hypoglycemia associated with erythroblastosis fetalis.

Hazeltine (1967) reported two infants with severe erythroblastosis fetalis who had severe hypoglycemia.

Driscoll and Steinke (1967) found that pancreases of Rh erythroblastic infants had significantly elevated insulin content when compared to controls and the same was true of infants of diabetic mothers.

Barret et al (1968) observed hypoglycemia in 31% of consecutively studied infants with moderate to severe erythroblastosis fetalis.

SERUM CREATININE AND SERUM UREA

During the last 50 years there has been an increasing interest in both abnormal and normal renal functions in the newborn period.

As early as 1920 Von Reuss commented that 34% of the neonates fail to pass urine in first twenty four hours of life, but that in health, micturition usually occurred two to three times during each of the first two days of life. Similarly Sherry and Kramer (1965) demonstrated that 23% of newborns passed urine within the first 24 hours while 99.4% had urination within the first 48 hours after delivery.

Jones (1972) reported urine out put of 0.5 - 5 ml/kg/hr on the first day of life and physiological oliguria in 7% healthy newborns. Similarly, Saili et al (1991) found urinary output of 1.02 ml/kg/hr in healthy neonates and physiological oliguria in 16.6% babies.

RENAL FUNCTION IN NEONATES

A. Structural Immaturity

Renal functions in neonate are relatively immature, in past related to structural immaturity. The glomerular development is ahead of tubular development and there is glomerulo-tubular imbalance. The glomerular

membrane is thinner and less well developed (Vernier, et al, 1962).

Increased plasma renin activity was found by Calcagno et al (1963) in the newborn babies. This explained the cause of increased renal vascular resistance and reduced renal plasma flow.

Moreover, the renal fraction of cardiac output is much smaller 4-6 percent in the first 12 hours and 8-10 percent in the first week when compared to adult (Dewes, 1968).

Gruskin et al (1976) after working on animal models concluded that renal vascular resistance was increased and renal plasma flow decreased in the immediate neonatal period.

B. Functional Immaturity

Polacek et al (1965) showed that the glomerular filtration rate was lower, and ability to concentrate urine and handle a given water load was limited in newborns.

Edelman (1969) pointed out that the fractional reabsorption of bicarbonate, phosphate, glucose and amino acids at the proximal tubule was incomplete.

CAUSES OF ARF IN NEONATES

The syndrome of acute renal failure is well defined in adults, but rarely occurrs in newborn infants.

In 1935, Craig described relative anuria and presence of abnormal urinary constituents in infants sustaining birth injury. In 1951, Jonsson described lower nephron nephrosis in asphyxia neonatorum. Clinical evidence for such a lesion was put forward by Doxiades et al (1952), Kessel et al (1955) and Malvorsen (1962).

Renal function during the first few days of life was studied systematically by Mc Cance and Widdowson (1954). They showed that infants born after protracted labour had increased breakdown of proteins, increased excretion of phosphates, low glomerular filtration and poor urea clearance.

The more frequent causes of renal failure in infants were diarrhoea and subsequent dehydration (Zuelzer et al, 1951), perinatal asphyxia (Bernstein and Mayer, 1961), severe haemorrhage both maternal and neonatal (Sankerkin et al, 1965), congenital anomalies (Lloyd , 1966), renal wein thrombosis (Aurelius, 1969), and septicemia (Saili et al, 1991).

Only a few studies have reported on the issues such as frequency, origin, and outcome of renal failure, in newborn babies. Alnold et al (1976) found the origin of neonatal renal failure as ischemic renal damage (38%), congenital renal and genitourinary tract lesions (32%) and multiple congenital anomalies (30%). Jones and co-workers (1979) found ischemic renal damage in 69 per cent neonates with renal failure, congenital renal lesions

in 25 percent and obstructive uropathy in 6 percent of his cases.

In his study on neonates with oliguria and uremia, Ellis et al (1982) found that 38% had prerenal uremia, 44% had renal insufficiency as a result of ischemic renal damage and 18% of infants had other causes of renal failure viz. toxic nephropathy, obstructive uropathy etc.

RENAL FUNCTION AND BIRTH ANOXIA

Perinatal anoxia remains a poorly recognised cause of renal failure. Gruenwald (1950) did not consider kidney as the site of pathology in asphyxic shock. However, Bernstein and Mayer (1961) have recognised a consistent association between the perinatal asphyxia and renal failure.

Kidney is very sensitive to oxygen deprivation. Within 24 hours of an ischemic episode renal insufficiency will occur. The condition is reversible , but prolonged ischemia can lead to irreverisible cortical or medullary necrosis (Rubin et al, 1962).

Anoxia causes renal ischemia by two methods : directly via hypoxemia and indirectly by causing shock, which decreases renal blood flow - owing to pooling and diversion of blood flow. Rudolph (1969) has shown a fall of 50 percent in renal blood flow in fetal lambs following anoxia.

The affected kidney (or kidneys) may recover

normal function or may show evidence of damage. This damage leads to :

a. Partially fibrosed kidney with diminished function (Wegner, 1969).

b. A non functioning completely fibrosed kidney (Belman et al, 1970).

c. Venovascular hypertension.

d. Nephrotic syndrome.

CLINICAL FEATURES

The cardinal clinical feature of renal failure is oliguria (Zuelzer, 1951; Bernstein, 1961; Lloyd, 1966). Its average duration was reported to be 12.7 days by Manley et al, (1968). Anuria is an omnious sign, suggesting bilateral renal dysgenesis, complete urinary tract obstruction or severe ischemic necrosis (Barret, 1971).

The infants are floppy, lethargic and seizures may occur. The kidneys may be palpably enlarged (Aurelins, 1969).

SERUM UREA - NORMAL BABIES

The most widely used tests to estimate renal function are blood urea, nitrogen and serum creatinine estimations. Unlike the creatinine levels, blood urea, nitrogen is influenced significantly by factors unrelated to glomerular filteration. Protein intake, increased incorporation of nitrogen during growth, alterations in liver functions and gastrointestinal absorption of nitrogen

as well as renal perfusion and urine flow will alter the blood levels of urea. It is only when the above variables are controlled does BUN provide an accurate indication of filtration rate (Greenhill et al, 1976).

A rise in the blood urea levels in the first three days of life indicate that the forces of production exceed that of excretion. During the first few days of life babies are in a state of hydropenia and it exaggerates tissue breakdown (Shiff, 1929, Mc Cance, 1936). Hydropenia curtails the ability of newborn child to excrete urea (Mc Cance and Young, 1941; Young and Mc Cance, 1942).

The initial fall which occurs after the preceding increase in blood urea levels may be due to utilization of urea for enzyme protein formation Giordance, 1963).

SERUM UREA LEVELS

Mc Cance (1954) in his study of blood urea in twelve full term infants reported 18.9 mg/dl as the average concentration in normal healthy infants at birth. Smith et al (1955) reported on concentration of urea in the blood of prematures, at birth and on the first day of life. At birth (cord blood) the average concentration of urea was 14.5 mg/dl and on the first day of life the value was 36.2 mg/dl.

Pincus et al (1956) observed mean plasma urea of 22±12 mg/dl in babies weighing between 650-1350 gms

and 19±1 mg/dl in babies weighing between 1440-1905 gms. The mean concentration of urea in the control group of infants (weighing between 2415-4020 gms) was 15±7 mg/dl. Authors also found that there was a trend towards higher values of blood urea at 24 hours as compared to reference values at birth.

SERUM CREATININE - NORMAL BABIES

The concentration of creatinine, one of the simple and commonly used indices of glomerular filtration rate (GFR) in children and adults, has been reported to be appreciably raised and variable during the first month of life (Sertel et al, 1973; Gruskin et al, 1976; Stonestreet et al, 1978).

The high plasma creatinine concentration at birth perhaps maternal in origin, and the decline in levels during the first month of life greatly limits the use of creatinine as an index of glomerular filtration in infants.

Since current methodology for the measurement of plasma creatinine levels include analysis of chromogens this may lead to false higher values in the first 10 days of life (Lauson, 1951). Increased tissue destruction and reduced glomerular filtration rate may alternatively account for the higher plasma creatinine values in first ten days of life. Reduction in tissue catabolism and improvement in glomerular filtration rate during the

first 3 months of life (Guignard et al, 1975) may account for the gradual decline and stabilization in plasma creatinine levels.

Plasma creatinine in first three months of life in the low birth weight infants was estimated by Stone street et al (1978). In the first ten days, mean plasma creatinine level was 1.3±0.07 mg/dl and the values ranged from 0.8 to 1.8 mg/dl. Beyond 1 month of age all values were below 1 mg/dl . An inverse relationship was found between plasma creatinine levels and post natal age.

Feldman and Guignard (1982) worked on plasma creatinine values in neonates in the first month of life, while they did not receive any drug. Plasma creatinine values during the first five days of life ranged from 2.124 to 0.1921 mg/dl. After day five plasma levels were fairly stable through out the first month with a mean value of 35±2 u mol/l (0.3955 ± 0.022 mg/dl).

Reference ranges for plasma creatinine during the first month of life have been worked by Rudd et al, (1983). They found an inverse relationship between plasma creatinine level and gestational age/postnatal age. Infants undergoing mechanical ventilation at 2 days age were found to have significantly raised creatinine levels.

BLOOD/SERUM UREA LEVEL IN SICK NEONATES

Dauber et al (1976) in their study of ARF consequent on perinatal anoxia found initial blood urea nitrogen (BUN) values ranging from 20 to 59 mg/dl.

Anand et al (1978) in a study on 'sick' neonates found the mean peak serum urea nitrogen (SUN) concentration to be 68 mg/dl (range : 25 to 115). In all patients ARF was secondary to a major perinatal disease viz. pneumonia, disorder e.g. hyaline membrane disease, meconium aspiration syndrome, haemorrhage or sepsis. Several had more than one cause contributing to higher SUN. Shock secondary to sepsis, hypoxia or haemorrhage was present in more than 60 percent of patients.

Norman et al (1976) found six percent of consecutive admissions of critically sick newborn infants to have developed intrinsic acute renal failure (20 out of 314 admissions). The mean blood urea nitrogen was 27 mg/dl with a range of 8 to 80 mg/dl.

Ellis et al (1982) reported blood urea nitrogen value of 32±20 mg/dl in pre-renal azotemia in immediate postnatal period, 39±19 mg/dl in pre-renal failure due to diarrhoea and dehydration, 46±28 mg/dl in ischemic renal damage consequent to birth anoxia and 46±46 mg/dl in other cases, viz. those who had toxic/obstructive uropathy.

SERUM CREATININE AND BIRTH ANOXIA

Dauber et al (1976) reported raised serum creatinine values in birth anoxic neonates who developed acute renal failure . The values ranged from 1.4 mg/dl to 6.2 mg/dl.

Anand et al (1978) in his study on sick neonates who developed ARF, found that the mean peak creatinine concentration was 3.3 mg/dl(range : 1.8 to 6.7 mg/dl). In all patients ARF was secondary to major perinatal disorder.

Normal et al (1979) made the diagnosis of presumptive ARF in 23 percent of total critically sick neonates admitted to intensive care unit. Of these only 6% were found to have intrinsic acute renal failure and their serum creatinine ranged from 1.2 to 8.8 mg/dl with a group mean of 2.5 mg/dl.

Ellis et al (1982) recorded causes of renal failure in 45 neonates with oliguria and uremia. In 44 percent of cases renal insufficiency was a result of ischemic renal damage. The mean serum creatinine level was 2.8 ± 1.8 mg/dl.

SERUM CREATININE AND SEPTICEMIA

In a recent study carried by Saili et al (1991) the incidence of acute renal failure in neonatal septicemia was reported to be 20% which tallies with the values (16.6%) reported by Griffin et al (1976). In septicemic neonates with acute renal failure, serum creatinine ranged from 1.2 to 2.2 mg/dl(Saili et al,1991).

MECHANISM OF ARF IN SEPTICEMIA

The possible mechanisms of sepsis causing acute renal failure are as follows :

1. Direct damage to blood vessels leading to disseminated intravascular coagulation and consequent renal tubular necrosis (Barret, 1971).
2. Possible role of myoglobinuria following renal damage by gram negative bacteria (Haptal, 1978).
3. Transient acute pyelonephritis (Rehman, 1981).
4. Shock like state due to gram negative septicemia (Anand et al, 1978; 1982).

RENAL FUNCTION IN ACUTE RESPIRATORY DISTRESS SYNDROME

A state of acute reversible renal insufficiency can occur in acute phase of idiopathic respiratory distress syndrome (Guignard et al, 1976). The author opined that the renal insufficiency observed in RDS is 'Pre renal' i.e. functional rather than secondary to parenchymal damage.

RENAL FUNCTION IN DIARRHOEA AND DEHYDRATION

Ellis et al (1982) reported increased level of serum creatinine and blood urea in neonate having ARF as a consequence of diarrhoea and dehydration.

Among the neonates who developed ARF, pre-renal uremia was present in 37.8%. In these infants serum creatinine was 2.1 ± 1.4 mg/dl and BUN was 39 ± 19 mg/dl.

SERUM BILIRUBIN

Though neonatal icterus is not a major cause of neonatal mortality in our country yet morbidity during

the neonatal period and post neonatal period is sufficiently severe to make early recognition and adequate management an important aspect of preventive pediatrics.

PHYSIOLOGY AND CHEMISTRY OF BILIRUBIN

In liver, bilirubin is conjugated by the action of glucuronyl transferase and is mainly converted to diglucuromide by ester formation (Cole and Lathe, 1953; Billing and Lathe, 1956).

Lathe (1956) suggested the term conjugated and unconjugated bilirubin for these two types of bilirubin occurring in the body. The terms unconjugated and conjugated are used respectively for free and ester forms. Conjugated bilirubin is water soluble whereas unconjugated is not.

Odell (1959) has shown that unconjugated bilirubin may be present in the plasma in two forms. The majority of bilirubin is bound to albumin and presents as albumin-bilirubin complex which gives a spectral absorption peak at 460 um. However, unconjugated bilirubin may also be present in free form which gives a spectral absorption peak of 420 um.

Conjugated bilirubin is excreted into bile canaliculi, from where it finds its way into the intestine. Conjugated bilirubin is not readily absorbed from intestine (Lester and Schmid, 1963) and is excreted from the body, by being broken into urobilinogen and sterco-bilinogen. Part of urobilinogen is reabsorbed and excreted again in

bile and also in the urine.

BILIRUBIN TOXICITY

Conjugated bilirubin is not neurotoxic. It is the unconjugated free bilirubin which causes brain damage. Free bilirubin acts upon central nervous system in two ways. Diamond and Schmid (1966) have shown that only unbound bilirubin can cross the blood brain barrier and consequently the amount of bilirubin transferred into the brain is determined by the magnitude of unbound fraction rather than by the concentration of total bilirubin in plasma.

Odell (1966) has shown that mitochondria can preferentially sequester bilirubin when suspended in bilirubin-albumin aqueous suspension. This can be prevented by addition of protein in adequate concentration. If the bilirubin level rises (administering salicylates/ sulmethoxazole to pregnant mother/neonates) or the protein level decreases, increased amount of bilirubin is sequestered in mitochondria leading to uncoupling of oxidative mechanism and brain injury i.e. kernicterus.

BILIRUBIN METABOLISM IN FETUS

Serum bilirubin tends to be low in fetal circulation and rises sharply in the newborn infant shortly after birth (Davidson et al, 1941; Fashena, 1948; Haia et al, 1953). Since both UDPG dehydrogenase and glucuronyl transferase are very low in fetal liver

(Lathe and Walker, 1958; Dutton, 1959; Gartner and Arias, 1963), the conjugation of bilirubin to its glucuromide form cannot occur in the fetus at a normal rate. This bilirubin is removed from the fetal circulation by transfer across the placenta to the maternal circulation (Schenkar et al, 1964) and eventually conjugated by maternal liver and excreted in her bile.

PHYSIOLOGICAL JAUNDICE

As soon as the cord is cut, the fetus looses the placental mechanism for the removal of bilirubin through the maternal liver and bile. As a result, there is moderate accumulation of unconjugated bilirubin in plasma, and this is usually referred to as "Physiologic jaundice". The neonate has reduced efficiency of bilirubin conjugating mechanism due to a marked deficiency of UDPG dehydrogenase and glucuronyl transferase activity (Lathe and Walker, 1958; Dutton, 1959 and Gartner and Arias, 1963).

There is an increased haematocrit level (Hb 17 mg/dl) and a decreased red blood cell life span in neonates (about 70 days, Pearson, 1967). This leads to a slight increase in the rate of bilirubin formation which under normal circumstances could be easily conjugated and excreted by liver, but for the deficiency of bilirubin conjugating mechanism.

ROLE OF GLUCORONYL TRANSFERASE INHIBITORS

In 1958, Lathe and Walker first reported that

serum from pregnant women inhibited the conjugation of bilirubin by liver slices. More detailed studies by Arias and his coworkers (Arias et al, 1964, Arias and Gartner, 1964 and Arias et al, 1965) have revealed that pregnant - 3 (alpha)- 20(beta) - diol isolated from breast milk and perhaps from certain type of maternal serum inhibited glucuronyl transferase and might be responsible for excessive jaundice in newborn infants.

PATHOLOGICAL HYPERBILIRUBINEMIA

Many disease states can alter the normal physiologic hyperbilirubinemia and lead to pathological hyperbilirubinemia of the newborn. Thus jaundice appearing on the 1st day or persisting after a week in term and 10-12 days in preterm is pathological.

Various disease states act at one or more of the following sites to cause pathological hyperbilirubinemia.

1. Increased Breakdown of Red blood cells

The most common cause of excessive haemolysis during neonatal period is erythroblastosis fetalis. Other causes include ABO incompatibility, glucose-6 phosphate dehydrogenase deficiency (Doxiadis et al, 1960; Lu et al, 1966), and at least a dozen genetically determined disturbances of the glycolytic cycle of red blood cells (Hsia, 1966). Excessive haemolysis can also occur if deficient but non haemolyzing babies or their mothers are exposed to certain drugs such as vitamin K,

Primaquine, sulfamethoxypridazine (Zinkham, 1967).

2. Interference with conjugation

This can be due to immaturity of liver, genetic defects and inhibitors of liver enzyme system.

Crigler and Najjar (1952) reported unconjugated hyperbilirubinemia in a group of infants who had extra-pyramidal symptoms. This was due to genetically determined absence of glucuronyl transferase.

Later Arias (1962) found partial or total deficiency of glucuronyl transferase in Gilbert disease.

Hargreaves et al (1962) Lokietz et al (1963) have shown that novobiocin is a potent inhibitor of glucuronyl transferase.

A greater degree of immaturity of glucuronyl transferase or its related enzyme UDPG dehydrogenase (Flodgaard and Brodersen, 1967) appears to be the greatest cause for excessive jaundice in new born and particularly in premature newborn.

3. Alteration of Protein binding

Silvermann (1956) found a high incidence of kernicterus in neonates receiving sulfisoxazole and penicillin. Odell (1959) showed it to be due to dissociation of bilirubin from albumin resulting in high concentration of free bilirubin.

4. Disturbances of Bilirubin excretion

The neonates particularly premarues are unable to fully excrete conjugated bilirubin in bile canaliculi

(Schenker et al, 1964).

5. Sepsis and Jaundice

Jaundice has long been recognized as a clinical manifestation of infection in newborn period and early infancy (Dunham, 1933; Silvermann, 1949; Smith, 1956; Nyhan, 1958). In these studies it is difficult to distinguish jaundice which might be definitely attributable to the septic process from that which might be encountered in idiopathic hyperbilirubinemia of newborn.

To estimate the real incidence of septicemic jaundice Bernstein et al (1962) designed a study which included seventy septicemic newborns who had jaundice and were more than 7 days old. Authors worked out an incidence of 13% for all types of bacterial sepsis. E. Coli and paracolon bacillus was responsible for thirty percent of all cases of jaundice.

CAUSATIVE/INFECTING AGENTS

These are mainly staphylococci , streptococci, and most of the enteric bacilli (Dunham, 1933; Nyham, 1958).

TYPE OF JAUNDICE

It has long been assumed (Silvermann et al, 1949) that in jaundice associated with sepsis, the elevation of bilirubin in serum is usually in the indirect reacting fraction. Sass Kortsak et al (1955) indicated that jaundice following severe infection was of regurgitative

type. Thurman (1960) demonstrated abnormal fragility in 28 of 42 infants with E. Coli sepsis. But this occurred only in 1 our of 26 cases of sepsis due to other organisms. Bernstein et al (1962) reported predominantly regurgitative jaundice in septicemia although unconjugated bilirubin levels were also excessively raised. A haemolytic phase probably preceded regurgitation in many cases.

Regurgitant jaundice could be due to extensive parenchymal damage (Bernstein et al, 1962) or due to pluging of extrahepatic or intrahepatic bile ducts as in inspissated bile syndrome.

6. Birth asphyxia and Jaundice

The liver plays a central role in the synthesis, degradation and regulatory metabolism of bilirubin. Due to asphyxia, liver may be so damaged that it is unable to perform the basic functions. The neonate is able to redistribute its blood flow so as to protect the vital organs (Peter et al, 1979) but at the cost of hypoxic liver damage.

Saili et al (1990) in his study on the effects of birth asphyxia on liver dysfunction found markedly elevated alkaline phosphatase, SGPT and SGOT. The total serum bilirubin level was comparable to that observed in the control group.

SERUM CALCIUM

Our understanding of antenatal serum calcium

and phosphorus metabolism is derived chiefly from animal data and distressingly small number of human material.

At birth more than 90% of total calcium and phosphorus is in the form of hydroxyapatite or bone salt (Shohl, 1939). Bone at term is relatively underminera-lized having half of the adult normal ash weight : dry weight ratio.

ANTENATAL PERIOD

The amount of calcium and phosphorus available for transport across the placenta depends largely on maternal factors. It is possible that fetus is normally passive. The following factors can be considered :

1. Hamilton et al (1936) isolated increased amount of a substance with bioassay characteristic of parathyroid hormone from the serum of pregnant women. Many investigators felt that pregnancy induces maternal hyperparathyroidism (Ludwig, 1962).
2. Role of diet and vitamin D : Adequate intake of calciferol by mother helps her to adapt to a wide range of calcium intake, so as to maintain normal fetal mineralization. Congenital rickets has been seen only in association with severe maternal osteo-malacia (Maxwell, 1930) in north China where mothers were totally deprived of calcium and calciferol by dietary and cultural patterns. Booher and Hausmann (1931), however, maintain that maternal nutrition has very little effect on fetal skeletal development.

3. Fetal response : Tetany lasting for several weeks has been seen in infants of hyperparathyroid mothers (Hartenstein and Gardner, 1966; Ertel et al, 1969). Conversely hyperparathyroidism has been reported in offspring of hypoparathyroid mothers (Aceto et al, 1964). Thus continuous exposure to excessive calcium concentration in utero may suppress fetal parathyroid function, whereas calcium lack may serve as a stimulus.

4. The role of placenta : Serum calcium level of human cord blood at birth exceeds simultaneously taken maternal venous samples (Economu-Mavrou and Mc Cance, 1958). This has led to a general conclusion that placenta actively transports calcium.

NEONATAL PERIOD

Mull et al (1936) correlated concentration of calcium in maternal serum with those obtained in cord blood. They found that the concentration of calcium was always higher in cord blood as compared to maternal serum. They also reported that maternal serum calcium level was lowest at six weeks prior to parturition and rose rapidly just before delivery.

It has been demonstrated by many observers (Bakwin, 1937) that a large intake of phosphorus in diet tends to depress the concentration of calcium in the serum of newborn infants during the first week of life. However, instances of hypocalcemia occurring on the first day of

life before any feed was administered to the newborn have been reported by Willi (1939) and Dodd (1949).

Hypocalcemia which occurs in the first 24 to 48 hours of life is termed "Early neonatal hypocalcemia" in contrast to hypocalcemia which occurs at the end of the first week called as "late neonatal hypocalcemia" .

Late neonatal hypocalcemia appears at the end of first week of life when food intake is well established and is associated with hyperphosphataemia.

Danzer et al (1939) found that immediately after birth, the concentration of calcium in infants serum was higher than the concentration in maternal serum.

Todd et al (1939) found instances of hypocalcemia in their study of 65 infants in whom they estimated the concentration of calcium in cord blood at birth and again on the third day of life by puncturing anterior fontanalle. Because blood was obtained on 3rd day of life, it was not clear when hypocalcemia actually occurred.

Gittleman et al (1956) estimated calcium level of neonates on the first day of life. They found that the incidence of hypocalcemia in mature infants born per vagina to mothers who had normal pregnancy and labour was 1.2%, while every infant born to a mother who had abnormal pregnancy and/or labour had hypocalcemia.

Gittleman et al (1956) found an increased incidence of hypocalcemia in mature infants born by

caesarean section, 14 percent when the indication for section was cephalopelvic disproportion and 37 percent when section was done for placenta previa, abruptio placentae, diabetes or eclampsia.

In a series of 111 infants, Gittleman et al (1956) found that the serum calcium concentration was less than 8 mg/dl in fifty five infants at some time during the first week of life. Hypocalcemia was inversely correlated with birth weight within the group ranging from 75% in 1080-1470 gm infants to 41% in those weighing 1920-2475 gms. The authors attributed this to following causes :

a. Immaturity of parathyroids.

b. Elevated cord level of cortisol derived from mother which has antagonistic activity to parathyroid hormone.

c. Starvation : This was so because the prematures are slow to establish adequate caloric intake. Fasting released endogenous phosphates from protein catabolism thereby producing hyperphosphataemia and hypocalcemia.

ADRENOCORTICOSTEROIDS AND SERUM CALCIUM

Adrenocorticosteroids influence calcium metabolism. Hopkins et al (1953) demonstrated that adrenocorticotrophin and cortisone depress the concentration of calcium in the serum of humans. Moeling and Steinbach (1954) found that administration of cortisone interfered with effectiveness of calcium therapy in hypoparathyroid states. Because concentration of these hormones increased in the serum of pregnant women, especially in the third

trimester, there was, thus sufficient evidence of trans-placental passage of these hormones. Author observed that it was concievable that hypocalcemia in the prematures could be caused by high concentration of these hormones.

HYPOCALCEMIA AND DIABETES

An association between maternal diabetes and early neonatal tetany has been noted by Craig (1958) and others. However, many such patients were also premature.

HYPOCALCEMIA AND BIRTH ANOXIA

Stoliar et al (1971) in their study on serum calcium levels in birth anoxic neonates found 26.76% incidence of hypocalcemia in full term infants and 58.33 percent in premature infants. Hypocalcemia was shown to be associated with acidosis in the first 24 hours of life and there after its correction.

Tsang et al (1973) in their study found that 37.6% percent of premature infants had serum calcium concentrations $<$7 mg/dl. They also found that low 1 minute Apgar scores was associated with low serum calcium values from 12 to 722 hours of age ($r = 0.409-0.559$, $p < 0.01$).

SERUM CALCIUM (First 48 hours)

There is a progressive fall of serum calcium from birth till about 36 hours or longer. Bakwin (1937) recorded the level at various intervals for the 1st 24

hours and found a steady fall of 1.43 mg/dl. Todd (1939) also recorded 1.3 mg/dl fall in the first two days.

Acharya and Payne (1965) reported a mean of 9.34 mg/dl calcium at birth which fell to 7.94 mg/dl at 48 hours.

NORMAL LEVELS

Normal serum calcium values have been worked out by many investigators in neonates. Bakwin (1937) reported 11 mg/dl, Denzer et al (1939) found 11.53 mg/dl, Todd et al (1939) reported 11.2 mg/dl, Bruck et al 10.59 mg/dl and Acharya et al (1965) 9.34 mg/dl (All cord blood values).

AIMS AND OBJECTIVES

This study was performed with the following aims and objectives :

1. To estimate the serum biochemical values in sick newborn babies on admission to paediatrics department.

2. To observe the magnitude of change in the biochemical values when the baby is clinically cured.

MATERIAL AND METHODS

The present study was carried out in the department of Paediatrics, Biochemistry and Obstetrics & Gynaecology, Maharani Laxmi Bai Medical College Hospital, Jhansi, Uttar Pradesh.

Babies delivered in labour room/operation theatre and subsequently admitted in the department of Paediatrics, as sick neonates requiring intensive care were included in this study. However, neonates directly admitted from out patient department or emergency were also included in the study.

SELECTION OF CASES

It included all the neonates (below 28 days of age) who were admitted on account of their illness in the department of Paediatrics.

Neonates were included in this study, irrespective of gestational age or birth weight. Neonates with the following diagnosis were considered for the present study :

1. Birth anoxia.
2. Septicemia.
3. Respiratory distress syndrome.
4. Intrauterine infection.
5. Acquired respiratory tract infection and pneumonia.

6. Meningitis.

7. Rh or ABO incompatibility.

8. Diarrhoea and dehydration.

9. Any other undiagnosed illness/underobservation.

Birth asphyxia was diagnosed when there was failure of establishment of spontaneous breathing at one minute or else there was unsatisfactory ventilation as evidenced by slow gasping breathing. All such neonates were born following traumatic, complicated or operative delivery and had one minute Apgar of 5 or less, and all required resuscitation at birth.

The diagnosis of birth asphyxia in the patients admitted directly from OPD/Emergency was entertained only when they were referred from other hospitals. However, the diagnosis of birth anoxia was also entertained if the parents gave a clear history pertaining to the absence of cry for more than five minutes and on examination the baby was found to have the signs of encephalopathy (Sarnat and Sarnat, 1976).

The septicemic neonates were divided into two groups, depending upon whether the onset occurred during the first 72 hours or later i.e. early septicemia and late septicemia, respectively.

The diagnosis of early septicemia was done when three of the following high risk factors were present.

1. Low birth weight (⩽2000 gms) or preterm baby.
2. Febrile illness in mother, during or within two weeks of delivery.

3. Foul smelling or meconium stained liquour amini.
4. Prolonged rupture of membranes of more than 24 hours duration.
5. More than 3 vaginal examinations during delivery.
6. Prolonged and difficult delivery with instrumentation.
7. Birth asphyxia and difficult resuscitation.

Above risk factors (minimum 3) along with the clinical features suggestive of septicemia were taken into account. They included alteration of behaviour and established feeding pattern of the baby, hypothermia, fever apnoiec spells and localizing features of infection.

Late onset septicemia was considered when the baby had localizing signs of sepsis viz. umbilical sepsis, furunculosis or any other systemic involvement and suddenly became lethargic, inactive with refusal to feed had fever, hypothermia or jaundice.

The diagnosis of respiratory distress syndrome was suspected when the respiratory rate was more than 60/minute in a quite resting baby along with intercostal indrawing and grunting. Cases of pneumonia were included when they had fever with tachypnoea (respiratory rate more than 60/minute) and showed pneumonic patches on X-ray chest.

C.S.F. proved cases of meningitis were included in the present study.

OBSTETRICAL HISTORY

This was recorded in all the sick neonates admitted, whether delivered in the hospital or in home and then subsequently admitted in this hospital.

This included the birth order of the baby, the date of last menstrual period, any miscarriages or history of habitual abortion.

Gestational age was calculated in completed weeks, from the first day of last menstrual period upto the time of delivery. The history of any chronic illness in the mother was also taken into account.

ANTENATAL, NATAL AND POST NATAL HISTORY

Mother was inquired about any illness, fever, or rashes during the first trimester of pregnancy. Similarly she was also questioned about the intake of any drug or exposure to radiation during the same period.

A history of maternal smoking, pre-eclampsia, eclampsia, leaking per vaginum, and tetanus immunization was also recorded.

For those babies delivered in medical college hospital, natal history was collected from the case records of the mother. In other cases, the duration of labour and mode of delivery was inquired into.

In post natal history any evidence of birth asphyxia was also inquired into.

EXAMINATION OF NEWBORN

All sick newborns were included in the study. In accordance with the history, thorough clinical examination was done in each case so as to reach to a relevant clinical diagnosis. Where necessary, appropriate laboratory investigations were carried out to substantiate the diagnosis.

Anthropometric measurements, viz, the weight, head circumference, chest circumference, crown heel length were taken on admission and were recorded in the predesigned proforma.

COLLECTION OF BLOOD SAMPLE

For the estimation of biochemical values, 5 ml blood was collected from a peripheral vein in a clean dried plain vial with anticoagulant, with due precautions to avoid haemorrhage and contamination. Blood was collected at the time of admission and at discharge.

All the glass wares used in the study were thoroughly washed and rinsed with distilled water and then dried. Blood samples were allowed to stand for clotting at room temperature, after an hour serum was separated by centrifugation at 10,000 rpm for 10-12 minutes. After centrifugation, clear serum at the top of sample was available for estimation purposes.

All the biochemical investigations viz. sugar, urea, creatinine, bilirubin and calcium in serum were

estimated on the same day in the department of Biochemistry using commercially available diagnostic kits of repute firms.

METHOD OF ESTIMATION

1. Method for glucose estimation in the serum (Barham and Trinder, 1972).

Serum glucose was determined by using glucose oxidase peroxidase method.

Principle

Glucose is oxidised by glucose oxidase to give gluconic acid and hydrogen peroxide. The hydrogen peroxide formed is broken down by peroxidase to water and oxygen. The later oxidises phenol which combines with 4-aminophenazone to give a red coloured complex. The intensity of the red coloured complex is proportional to the concentration of glucose in specimen under test.

The intensity of the coloured complex is measured colorimetrically at 515 nm (500-530 nm).

Reagents and Materials used

a. Commercially prepared kit for glucose estimation.
b. Water bath ($37^{o}C$).
c. Centrifuge machine.
d. Photoelectric colorimeter with filters in the range of 500-530 nm.
e. Clean dry test tubes, pipettes and micropipettes.

Procedure

The method required 1 to 10 dilution of test samples and standard (100 mg/dl) i.e. 0.1 ml of serum or standard and 0.9 ml of distilled water.

Following solutions were pipetted into three test tubes labelled as Test (T), Standard (S) and Blank(B).

Reagents	Test (T)	Standard (S)	Blank (B)
Glucozyme working reagent	5.0 ml	5.0 ml	5.0 ml
Serum (diluted 1 to 10)	0.25 ml	-	-
Standard (diluted 1 to 10)	-	0.25 ml	-
Distilled water	-	-	0.25 ml

The contents in the test tube were mixed well and placed in a water bath at 37°C for 15 minutes.

The optical density of the test and standard were measured against blank at 515 nm (range 500-530 nm).

Calculation

The following formula was used to calculate the concentration of glucose in the test specimen.

$$\frac{O.D.\ (T)}{O.D.\ (S)} \times 100 = \text{Glucose concentration (mg/dl)}.$$

2. Method for urea estimation in the serum (Natelson et al, 1951).

Urea was estimated by using end point DAM (Diacetylmonoxime) method. For this commercially prepared kit was used.

Principle

Urea reacts with diacetylmonoxime in hot acidic medium producing a specific pink coloured complex. The presence of ferric ions and other activators intensify the colour. The intensity of the complex is measured colorimetrically at 520 nm (range 510-540 nm) and is proportional to the concentration of urea nitrogen in the specimen under test.

Reagents and Material used

1. Commercially prepared kit for urea estimation.
2. Centrifuge machine.
3. Water bath (100°C).
4. Photoelectric colorimeter with filters in the range 510-540 nm.
5. Test tubes, pipettes and micropipettes.
6. Stop watch.

Procedure

The method uses a 1 to 20 dilution for test sample and standard. Three test tubes were taken and labelled as Test (T), Standard (S) and Blank (B).

Reagents	Test (T)	Standard (S)	Blank (B)
Colour reagent(Mix equal volume of reagent I & II)	3.00 ml	3.00 ml	3.00 ml
Acid reagent II	2.00 ml	2.00 ml	2.00 ml
Serum diluted 1:20 with distilled water(0.1 ml serum and 1.9 ml distilled water)	0.25 ml	-	-
Urea nitrogen standard (use 1 to 20 diluted ortho urea nitrogen standard working 20 mg/dl	-	0.25 ml	-
Distilled water	-	-	0.25 ml

The contents were mixed thoroughly and placed in boiling water bath for exactly 10 minutes.

After cooling the test tubes in running tap water, the optical density (OD) of test and standard was measured against blank at 520 nm. Readings were taken within 30 minutes.

Calculations

The serum urea nitrogen (SUN) was calculated using the following formula :

$$\frac{O.D.\ (T)}{O.D.\ (S)} \times 20 = \text{Urea nitrogen concentration (mg/dl).}$$

Urea nitrogen was expressed as urea by the use of the following formula

Urea (mg/dl) = Urea nitrogen(SUN) (mg/dl) x 2.14

3. Method for creatinine estimation in the serum (Bonsnes and Taussky, 1945).

Creatinine was determined by using Jaffe reaction. For this commercially prepared kit was used.

Principle

Creatinine in a protein free solution reacts with alkaline picrate and produces a red coloured complex, which is measured colorimetrically.

Reagents and Materials Required

1. Commercially prepared kit for creatinine estimation.
2. Stop watch.
3. Water bath.

4. Photoelectric colorimeter with filters in the range of 500-525 nm.

5. Pipettes and micropipettes and test tubes

Procedure : Step_I_

1. Preparation of working standard solution : For this 0.1 ml of stock creatinine standard was diluted by adding 9.9 ml of distilled water and mixed well.

2. Deproteinization of test sample was done by mixing

- Serum 1 ml
- Distilled water 1 ml
- Picric acid 6 ml

The mixture was mixed well, kept in boiling water bath for exactly 1 minute and cooled immediately under running tap water and centrifuged.

Step_II

	Blank (B)	Standard (S)	Test (T)
Supernatant from step I	-	-	4.00 ml
Working standard	-	1.00 ml	-
Distilled water	1.00 ml	-	-
Reagent I : Picric acid	3.00 ml	3.00 ml	-
Reagent II: Sodium hydroxide - 0.75 N	1.00 ml	1.00 ml	1.00 ml

Contents of the test tubes were mixed well and allowed to stand at room temperature exactly for 20 minutes before measuring the optical density of blank(B), Standard (S) and Test (T) against distilled water on a colorimeter with a green filter (520 nm).

Calculation

Concentration of creatinine in the serum was calculated by the formulae :

$$\frac{\text{O.D. of Test} - \text{O.D. of Blank}}{\text{O.D. of Standard} - \text{O.D. of Blank}} \times 3.0 = \text{Concentration of creatinine in test serum(mg/dl).}$$

4. Method for serum Bilirubin estimation (Malloy and Evelyn, 1937).

Principle

Direct (conjugated) bilirubin couples with diazetized sulfanilic acid forming azobilirubin, a red purple coloured product in acidic medium.

Indirect (unconjugated) bilirubin is diazotised only in the presence of its dissolving solvent(Methanol). Thus red purple coloured azobilirubin produced in the presence of methanol represent both direct and indirect fraction of total bilirubin. Difference of total and direct bilirubin is indirect bilirubin. Intensity of red purple colour so developed is measured colorimetrically and it is proportional to the concentration of appropriate fraction of bilirubin.

Reaction can be represented as under :

Bilirubin + Diazotized sulfanilic acid

$\downarrow H^+$

Azobilirubin

$\downarrow H^+$

Red purple colour

(% max : 540 nm)

Reagents and Material required

1. Commercially prepared kit for Bilirubin estimation.
2. Photoelectric colorimeter with filters of 540-550 nm.
3. Test tubes and pipettes.

Procedure

		T_1	T_2
1.	Serum (ml)	0.2	0.2
2.	Distilled water (ml)	1.8	1.8
3.	Reagent 3 : Diazo blank (ml)	-	0.5
4.	Diazo reagent (ml)	0.5	-
5.	Reagent 4(Methanol)(ml)	2.5	2.5

The test tubes T_1 and T_2 were mixed well and kept in dark at room temperature for 30 minutes and O.D. wasread against distilled water in a colorimeter at 540-550 nm.

Standard : The O.D. of reagent 5 (artificialstandard) (10 mg/dl bilirubin) was read against distilled water on a colorimeter at 540-550 nm.

Calculation

$$\text{Total serum Bilirubin} = \frac{\text{O.D.}(T_1) - \text{O.D.}(T_2)}{\text{O.D. of Standard}} \times 10 \text{ mg/dl}$$

5. Method for serum calcium estimation
(Connerty and Briggs, 1966).

Principle

Calcium in serum reacts with O-cresolphthalein complexone in alkaline medium forming purple coloured

complex which is measured by colorimeter using yellow filter (wave length 570 nm).

Reagent and Materials required

1. Commercially prepared kit for serum calcium estimation.(
2. Pipettes and test tubes.
3. Photoelectric colorimeter having filter 560-580 nm.

Procedure

1. Test tube labelling was done, one each for Blank(B), Standard (S) and Test (T).
2. 3.0 ml calcium colour reagent was taken in all test tubes.
3. 1.0 ml AMP buffer was added in each test tube.
4. Then 0.05 ml serum was taken in T-test tube and 0.05 ml working colour standard in S-standard test tube.
5. Mixing was done by lateral shaking and all tubes were allowed to stand at room temperature for 5 minutes.
6. Optical density was measured against distilled water adjusted to zero at 570 nm on the colorimeter.
7. Concentration of serum calcium in serum was calculated as under :

$$\frac{\text{O.D. of Test} - \text{O.D. of Blank}}{\text{O.D. of Standard} - \text{O.D. of Blank}} \times 10 = \text{Concentration of serum calcium (mg/dl).}$$

O B S E R V A T I O N S

The present study was conducted in the department of Paediatrics, M.L.B. Medical College, Jhansi to determine the serum level of various biochemical parameters in critically sick neonates and to observe the magnitude of change in these values subsequent to clinical cure at the time of discharge.

The subjects for this study were 64 sick babies admitted in the neonatology section of Paediatrics department between October, 1993 to Aug, 1994.

The study included 45 male and 19 female cases.

TABLE I : Frequency distribution of cases according to sex.

Sl. No.	Sex of baby	No.of cases	Percentage
1.	Male	45	70.31
2.	Female	19	29.69
	Total	64	100.00

The sex wise distribution of cases showed preponderance of male babies (70.31%) in the sample.

Cases were further classified into following subgroups according to their specific illness.

a. Birth asphyxiated neonates.
b. Septicemic neonates.
c. Neonates with miscellaneous ailments.

The last group comprised of four cases, two each of acute respiratory distress syndrome, a case of congenital malaria and another of epidermolysis bullosa letalis.

TABLE II : Frequency distribution of cases according to clinical diagnosis.

Sl. No.	Diagnosis	No.of cases	Percentage
1.	Birth Asphyxia	21	32.81
2.	Septicemia	39	60.94
3.	Miscellaneous(others)	4	6.25
	TOTAL	64	100.00

There was 21 cases (32.81%) in the birth asphyxiated group as against 39(60.94%) in the septicemic group.

BIRTH ASPHYXIATED BABIES

TABLE III : Frequency distribution of birth asphyxiated babies according to sex.

Sl. No.	Sex of baby	No.of Cases	Percentage
1.	Male	11	52.38
2.	Female	10	47.62
	Total	21	100.00

This group of neonates comprised of 21(32.81%) babies . There were ten female and eleven male babies in this group.

TABLE IV : Distribution of cases according to gestational age.

Sl. No.	Group	No.of cases	Percentage
1.	Preterm	9	42.86
2.	Full term	11	52.38
3.	Post term	1	4.76
	Total	21	100.00

These babies were classified according to gestational age into preterm (<37 weeks), full term (37-41 weeks), and post term (>41 weeks) groups. There were 11 (52.38%) cases in full term group, 9(42.86%) cases in preterm group and only one (4.76%) case was in post term group (Table IV).

TABLE V : Frequency distribution of birth asphyxiated babies that survived and those who died.

Sl. No.	BIRTH asphyxiated babies	No.of cases	Percentage
1.	Improved	11	61.11
2.	Died	7	38.89

Of the 21 birth asphyxiated babies admitted to the paediatric ward, 3 left the study during the course of their treatment. Out of the remaining 18 babies, seven (38.89%) died during the study period and 11 (61.11%) improved and survived (Table V).

SEPTICEMIC BABIES

TABLE VI : Frequency distribution of septicemic babies according to sex.

Sl. No.	Sex of baby	No.of cases	Percentage
1.	Male	31	79.49
2.	Female	8	20.51
	Total	39	100.00

This group of babies comprised of 39 neonates (60.94%). There were 31 (79.49%) males and 8(20.51%) female babies in this group (Table VI).

TABLE VII : Frequency distribution of cases according to gestational age.

Sl. No.	Group	No.of cases	Percentage
1.	Preterm	10	25.64
2.	Full term	29	74.36
3.	Post term	-	-
	Total	39	100.00

This group included 10 preterm (25.64%) and 29 (74.36%) full term babies . None of the baby was post term (Table VII).

TABLE VIII : Frequency distribution of septicemic babies that survived and those who expired.

Sl. No.	Septicemic neonates	No.of cases	Percentage
1.	Improved	24	68.57
2.	Expired	11	31.43

In this group four babies dropped out from the study. Of the remaining 35 babies, 24 (68.57%) babies improved and rest 11(31.43%) babies expired.

SERUM GLUCOSE

BIRTH ANOXIC NEONATES

TABLE IX : Showing mean $\pm$SD values of glucose (mg/dl) at admission and discharge in birth anoxic babies.

Sl. No.	Birth Anoxic baby	Serum Glucose Mean$\pm$S.D.	p value
1.	Admission(21)	37.05$\pm$20.22	<0.05
2.	Discharge(11)	50.83$\pm$11.83	

't' = 2.126, d.f. = 30 (Degree of freedom)

On comparison of mean serum glucose value at admission and discharge , it was observed that serum glucose was lower at admission (37.05$\pm$20.22 mg/dl) than at discharge (50.83$\pm$11.83 mg/dl and the difference was statistically significant ($p < 0.05$) (Table IX).

TABLE X : Showing mean ±S.D. values of serum glucose (mg/dl) in different gestational age groups at admission.

Sl. No.	Groups	Serum glucose Mean±S.D.
1.	Preterm (9)	29.50±19.06
2.	Full term(11)	44.19±19.37
3.	Post term (1)	26.45

The overall mean glucose value observed at admission during this study was 37.05±20.22 mg/dl. The mean glucose values observed for various gestational age groups i.e. preterm, and full term were 29.50±19.06 mg/dl and 44.19±19.37 mg/dl respectively, but the difference was statistically not significant (p >0.1) (Table X).

SEPTICEMIC NEONATES

TABLE XI : Showing mean ±S.D. values of glucose(mg/dl) at admission and at discharge in septicemic neonates.

Sl. No.	Septicemic babies	Serum glucose Mean ±S.D.	p value
1.	Admission	46.92±25.13	<0.001
2.	Discharge	76.29±16.93	

't' = 5.1380, d.f. = 61 (Degree of freedom)

On comparison of mean serum glucose in septicemic neonates it was observed that serum glucose was lower at admission (46.92±25.13 mg/dl) than at discharge(76.29± 16.93 mg/dl) (Table XI).

TABLE XII : Showing mean ±S.D. values of serum glucose in septicemic neonates in different gestational age groups at admission(mg/dl).

Sl. No.	Group	Serum glucose Mean±S.D.
1.	Preterm (10)	34.95±20.09
2.	Full term (29)	51.30±25.25

't' = 0.22, p >0.8, d.f. = 37.

The over all mean glucose values observed at admission in septicemic neonates in this study was 46.92±25.13 mg/dl. The mean glucose values observed for various gestational age groups i.e. preterm and full term were 34.95±20.09 mg/dl and 51.30±25.25 mg/dl respectively, but the difference was statistically insignificant (p >0.8) (Table XII).

SERUM CALCIUM VALUES

BIRTH ANOXIC BABIES

TABLE XIII : Showing mean ±S.D. values of serum calcium (mg/dl) in birth anoxic babies at admission and discharge.

Sl. No.	Birth Anoxic babies	No.of cases	Serum calcium Mean ±S.D.	p value
1.	Admission	21	7.466±1.974	<0.02
2.	Discharge	11	9.009±1.362	

't' = 2.3424, d.f. = 30,

Table XIII shows that the mean values of serum calcium in birth anoxic babies at admission (7.466±1.974 mg/dl) was lower than that of discharge (9.009±1.362 mg/dl)

and on applying student 't' test, the difference between the paired mean was significant (p $<$0.02) (Table XIII).

TABLE XIV : Showing mean ±S.D. values of serum calcium levels in birth anoxic babies in various gestational age groups at admission.

Sl. No.	Group	No.of cases	Serum calcium Mean±S.D.
1.	Preterm	9	7.055±1.772
2.	Full term	11	7.754±2.072
3.	Post term	1	8.00

The overall mean calcium value observed during this study in birth anoxic babies at admission was 7.466±1.974 mg/dl. The mean serum calcium values observed for various gestational age groups at admission in preterm and full term babies were 7.055±1.772 and 7.754±2.072 mg/dl respectively. On applying student't' test the difference was not statistically significant (p $<$0.4) (Table XIV).

SEPTICEMIC BABIES

TABLE XV : Showing mean ±S.D. of serum calcium values in septicemic neonates at admission and discharge (mg/dl).

Sl. No.	Septicemic babies	No.of cases	Serum calcium Mean±S.D.	p value
1.	Admission	39	7.752±1.526	$<$0.001
2.	Discharge	24	9.304±0.999	
	't' = 4.5076,	d.f. = 61		

Table XV shows that the mean serum calcium value at admission of septicemic neonates was 7.752±1.526 mg/dl which was lower than that at discharge (9.304±0.999 mg/dl) and the difference was found to be statistically significant (p <0.001).

TABLE XVI : Showing mean ±S.D. values of serum calcium in septicemic babies in various gestational age groups at admission.

Sl. No.	Group	No.of cases	Serum calcium Mean±S.D.	p value
1.	Preterm	10	7.22±1.302	>0.5
2.	Full term	29	7.935 ±1.554	

't' = 0.6922, d.f. = 37

The overall mean serum calcium value observed during this study in septicemic neonates at admission was 7.752±1.526. The serum calcium level was higher in term septicemic babies at admission (7.93±1.55) as compared to preterm septicemic babies (7.22±1.30 mg/dl), but the difference was not statistically significant(p >0.5) (Table XVI).

SERUM UREA NITROGEN AND SERUM UREA

BIRTH ANOXIC BABIES

TABLE XVII : Showing mean±S.D. of serum urea nitrogen and serum urea(mg/dl) in birth asphyxiated babies at admission and at discharge.

Sl. No.	Birth anoxic babies	No.of cases	S.Urea Nitrogen Mean ±S.D.	Serum Urea Mean±S.D.
1.	Admission	21	39.545±23.938	84.632±51.248
2.	Discharge	11	16.483±18.016	33.682±38.990

't' = 2.8217, p < 0.001, d.f. = 30

Above table XVII shows that the mean value of serum urea nitrogen in birth asphyxiated babies at admission was higher than that at discharge. This difference was statistically highly significant($p < 0.001$)

TABLE XVIII : Showing mean±S.D. values of serum urea nitrogen and serum urea in birth asphyxiated babies in various gestational age groups at admission(mg/dl).

Sl. No.	Groups	No.of cases	S.Urea nitrogen Mean±S.D.	Serum Urea Mean±S.D.
1.	Preterm	9	39.77±21.938	85.148±46.989
2.	Full term	11	36.887±25.022	78.935±53.547
3.	Post term	1	66.70	142.738

The overall mean serum urea nitrogen and serum urea at admission was 39.545 mg/dl and 84.632 mg/dl respectively. The mean serum urea nitrogen and serum urea values were higher in preterm babies than full term babies. Mean serum urea nitrogen value at admission in preterm babies was 39.77±21.938 mg/dl as against in full term babies (36.887±25.022 mg/dl). However, the difference was statistically not significant ($p > 0.5$).

SEPTICEMIC NEONATES

TABLE XIX : Showing mean±SD of serum urea nitrogen and serum urea in septicemic babies at admission and discharge (mg/dl).

Sl. No.	Septicemic babies	No.of cases	S. urea nitrogen Mean±S.D.	Serum Urea Mean±S.D.
1.	Admission	39	25.594±19.501	54.768±41.732
2.	Discharge	24	11.534±8.862	25.70±18.831

Table XIX shows that the mean serum urea nitrogen and serum urea values in critically ill septicemic babies at admission was higher than at discharge. The mean at admission was 54.768 mg/dl which fell to 25.70 mg/dl at discharge and the difference was statistically significant ('t' = 2.55, d.f. = 37, $p < 0.02$).

TABLE XX : Showing mean±S.D. values of serum urea nitrogen and serum urea in septicemic neonates in various gestational age groups at admission (mg/dl).

Sl. No.	Group	No.of cases	S.Urea nitrogen Mean±S.D.	Serum urea Mean± S.D.
1.	Preterm	10	22.622±11.429	48.406±24.461
2.	Full term	29	26.618±21.501	56.963±46.0116

't' = 0.572, $p > 0.5$, d.f. = 37

The over all mean serum urea nitrogen and serum urea in septicemic neonates in this study was 25.59 mg/dl and 54.76 mg/dl respectively. The values were slightly higher in the term septicemic babies as compared to preterm babies, but the difference was not statistically significant ($p > 0.5$) (Table XX).

SERUM CREATININE VALUES

BIRTH ANOXIC BABIES

TABLE XXI : Showing mean±S.D. values of serum creatinine (mg/dl) in birth asphyxiated babies at admission and discharge.

Sl. No.	Birth Anoxic babies	No.of cases	Serum creatinine Mean±S.D.	p value
1.	Admission	21	2.079 ±0.903	<0.001
2.	Discharge	11	0.981 ±0.668	

't' = 3.574, d.f. = 30.

Table XXI shows that the mean value of serum creatinine in birth anoxic babies at admission (2.079± 0.903 mg/dl) was higher than at discharge (0.981 ± 0.668 mg/dl). The difference was statistically highly significant (p <0.001).

TABLE XXII : Showing mean ±S.D. values of serum creatinine in birth asphyxiated babies in various gestational age groups at admission(mg/dl).

Sl. No.	Groups	No.of cases	Serum creatinine (mean ±S.D.
1.	Preterm	9	2.168 ±0.713
2.	Full term	11	1.930 ±1.025
3.	Post term	1	2.9

The overall mean serum creatinine value observed during this study in birth asphyxiated babies at admission

was 2.079±0.9034 mg/dl. The mean serum creatinine observed for various gestational age groups at admission in preterm and term babies were 2.168 ±0.713 and 1.930 ±1.025 mg/dl respectively and the difference was statistically insignificant (p ⟨0.2).

The only post term baby in this study had serum creatinine value of 2.9 mg/dl.

SEPTICEMIC NEONATES

TABLE XXIII : Showing mean±S.D. of serum creatinine values in septicemic neonates at admission and discharge (mg/dl).

Sl. No.	Septicemic babies	No.of cases	Serum creatinine Mean±S.D.
1.	Admission	39	1.572±0.897
2.	Discharge	24	0.820±0.399

't' = 4.0877, p ⟨0.001, d.f. = 61

Table XXIII shows that the mean serum creatinine value at admission of septicemic neonates was 1.572±0.897 mg/dl which was higher than that at discharge (0.820±0.399 mg/dl) and the difference was found to be statistically highly significant (p ⟨0.001).

TABLE XXIV: Showing mean±S.D. values of serum creatinine in septicemic babies in various gestational age groups at admission (mg/dl).

Sl. No.	Group	No.of cases	Serum creatinine Mean±S.D.
1.	Preterm	10	1.767±0.679
2.	Full term	29	1.505±0.8916

't' = 0.8507, p > 0.4, d.f. = 37

The overall mean serum creatinine value observed during the study in septicemic neonates at admission was 1.572±0.897 mg/dl. The serum creatinine level was higher in preterm babies as compared to full term babies but the difference was not statistically significant (p > 0.4) (Table XXIV).

SERUM BILIRUBIN VALUES

BIRTH ANOXIC NEONATES

TABLE XXV : Showing mean±S.D. serum bilirubin values (mg/dl) in birth anoxic babies at admission and discharge.

Sl. No.	Birth Anoxic babies	No.of cases	Serum bilirubin Mean±S.D.
1.	Admission	21	7.362±5.687
2.	Discharge	11	3.845±1.831

't' = 2.065, p < 0.05, d.f. = 30

It was observed from the study that mean serum bilirubin in birth anoxic babies was higher at admission than at discharge. The mean value at admission was 7.362 mg/dl whereas it was 3.845 mg/dl at discharge (Table XXV).

TABLE XXVI : Showing mean ± S.D. values of serum creatinine (mg/dl) in birth anoxic neonates in various gestational age groups at admission.

Sl. No.	Groups	No.of cases	Serum Bilirubin Mean ± S.D.
1.	Preterm	9	7.711±4.92
2.	Full term	11	6.655±6.275
3.	Post term	1	12.0

The overall mean serum bilirubin value observed during this study in birth anoxic babies at admission was 7.362 mg/dl. The mean serum bilirubin values observed for various gestational age groups at admission in preterm and full term babies were 7.711 mg/dl and 6.655 mg/dl respectively. The difference was however not statistically significant (p >0.6, 't' = 0.415).

In the post term group there was only one neonate whose serum bilirubin level was 12 mg/dl.

TABLE XXVII : Showing mean±S.D. of serum bilirubin values in septicemic neonates at admission and discharge (mg/dl).

Sl. No.	Septicemic babies	No.of cases	Serum bilirubin Mean±S.D.	p value
1.	Admission	39	5.956±4.876	
				< 0.001
2.	Discharge	24	2.068±1.691	

't' = 3.963, d.f. = 61.

Table XXVII shows that the mean serum bilirubin levels in septicemic neonates at admission were higher than at discharge. The mean value at admission was 5.956 mg/dl whereas it was 2.068 mg/dl at discharge.

TABLE XXVIII : Showing mean±S.D. values of serum bilirubin in septicemic neonates in various gestational age group at admission (mg/dl).

Sl. No.	Groups	No.of cases	Serum bilirubin Mean ± S.D.
1.	Preterm	10	6.613±4.1445
2.	Full term	29	5.73 ±5.085

't' = 0.496, p > 0.6, d.f. = 37

The overall mean serum bilirubin level at admission in septicemic neonates was 5.956 ±4.876 mg/dl . The mean value in preterm septicemic babies was 6.613 mg/dl which was higher than seen in full term babies at admission. The difference was however, not statistically significant (p >0.6) (Table XXVIII).

D I S C U S S I O N

D I S C U S S I O N

The present work was carried out to study the serum level of glucose, urea, creatinine, calcium and bilirubin in critically sick neonates at admission and the subsequent change in these variables at discharge. The study was conducted at M.L.B. Medical College, Jhansi in the department of Pediatrics in collaboration with department of Obstetrics and Gynaecology from October, 1993 to Aug., 1994. The estimation of biochemical values was done in the department of Pediatrics.

At admission weight and sex of the baby was recorded and a thorough clinical examination of the baby was carried out. The gestational age was calculated by counting the number of weeks from the first day of last menstrual period till the date of the birth of baby.

Statistical analysis was done to derive mean $\pm$S.D. values of glucose, calcium, urea, urea nitrogen, creatinine and bilirubin in sick babies at admission and at discharge. Besides these, mean $\pm$ S.D. values were also calculated in various gestational age groups. Paired values were compared using the student 't' test and significance of differences (p value) were noted.

Based on observation depicted in various tables, inferences were drawn and these have been discussed in details.

There was a preponderance of male sick babies (70.3%) in the sample group.

The study group was further subdivided into following subgroups according to their specific illness.

a. Birth asphyxiated babies.

b. Septicemic neonates.

c. Neonates with miscellaneous ailments.

The birth asphyxiated group included 21(32.81%) cases as against 39(60.94%) cases in the septicemic group. There were 4 babies with miscellaneous ailments The septicemic and birth asphyxiated babies were again subdivided into three groups depending upon their gestational age.

There were 9(42.86%) Preterm babies, 11 (52.38%) full term and 1(4.76%) post term baby in the birth asphyxiated group. Similarly in the septicemic group there were 10(25.64%) preterm, and 29(74.36%) full term babies. There was no post term baby in the septicemic group.

The mortality was 38.89 percent in the birth asphyxiated group and 31.43 percent in the septicemic babies.

In the present study the overall mean serum glucose at admission in the critically sick neonates irrespective of birth weight, gestational age and clinical diagnosis was 43.31±24.24 mg/dl. In contrast to this, Sharma et al (1993) in her study of serum glucose level in healthy neonates reported a mean value of 63.08±22.84 mg/dl in newborns irrespective of gestational age, sex or birth weight. Similarly, Acharya and Payne (1965) observed a higher mean value of blood glucose of 73 mg/dl in healthy newborn babies. However, Bhalla et al (1977) reported blood glucose value of 53 mg/dl in healthy neonates.

The lower mean value in sick neonates may have been due to increased utilization of glucose due to increased stress of illness, coupled with delay in initiating feeding and also owing to small quantity of feeds being accepted by critically ill babies during the first few days of life (Baens et al, 1963).

Relation with birth asphyxia

The serum glucose value in birth asphyxiated babies irrespective of gestational age at admission was 37.05±20.22 mg/dl in the present study.

Harris et al (1974) in his classical study on the effect of hypoxemia on blood glucose observed that hypoxemia has the universal effect of decreasing the blood glucose through out the first seventy four hours of life, although with less effect on preterm appropriate

for(AGA) gestation and small for gestational age babies (SGA).

In the present study the mean glucose level in asphyxiated babies who were admitted at 3-4 hours of age was 45.189±23.962 mg/dl. It was 41.01±16.45 mg/dl in asphyxiated babies who were admitted at three or four days of age.

Harris et al (1974) reported a mean blood glucose value of 37.5±1.8 mg/dl and 37.8±5.1 mg/dl respectively in full term and preterm asphyxiated babies at 3 hours of age.

The higher value of serum glucose at 3-4 hours of age in the present study could be accounted for better care of the mother during perinatal period and also by the fact that many mothers were receiving 5% dextrose solution intravenously at the time of child birth.

The serum glucose value in babies admitted at the age of 3-4 days in the present study was lower than observed in those admitted at the age of 1 day. The difference was statistically significant. This is in accordance with studies in healthy babies where the blood glucose was found to be the lowest at 3 hour and then on 3-4th day of life.

Reduced blood glucose value were also observed by Lubchenco et al (1971) in birth asphyxiated babies. The author concluded that decreased glucose values were due to reduced energy reserves in neonates with intra-

uterine growth retardation and the increased utilization of carbohydrates during birth hypoxia.

b. Relation with Septicemia

In the present study, the mean glucose value at admission in septicemic babies, irrespective of gestational age was 46.92±25.13 mg/dl.

Yeung (1970) studied the blood glucose values at admission in septicemic neonates. The mean glucose value was 53.83±27.10 mg/dl at admission.

The lower value in present study could be attributed to the delay in reporting of the sick babies to this hospital, and the practice of delayed breast feeding of babies by their mothers due to social and cultural taboos.

c. Correlation of serum glucose with gestational age in sick neonates

1. The serum glucose in septicemic preterm babies was 34.95±20.09 mg/dl as against 51.30±25.25 mg/dl in septicemic term babies. The difference was statistically not significant.
2. In birth anoxic babies lower serum glucose was found in preterm (29.5±10.22 mg/dl) as compared to term babies (44.19±19.37 mg/dl), but the difference was not statistically significant.

Similarly in the healthy babies the blood glucose tends to be lower in the prematures as compared to mature

babies (Cornblath et al, 1959, Brown and Wallia, 1963 and Haworth, 1965). Vegad et al (1974) studied serum glucose levels in newborns and found lower values in prematures (77.30 mg/dl) in comparison to full term babies (84.48 mg/dl).

It is well known that the fetus builds up its stores of glycogen and fat late in pregnancy which is eventually utilized by the body from birth until oral nutrition becomes adequate. Thus a preterm baby is deprived of its liver glycogen stores, and so its blood glucose level is expected to fall as soon as its available meagre energy sources are utilized. Infection tends to increase the utilization of glucose leading to still lower levels of blood glucose in premature babies. If in utero anoxia or birth asphyxia occurs, the liver glycogen stores are further depleted.

CHANGES IN SERUM GLUCOSE FROM ADMISSION TO DISCHARGE

TABLE XXIX : Showing significance of difference in serum glucose values at admission and at discharge in birth asphyxiated and septicemic babies (mg/dl).

Sl. No.	Outcome	At admission Mean±S.D.	At discharge Mean±S.D.	p value
1.	Birth anoxia	37.05±20.22	50.83±11.83	<0.05
2.	Septicemia	46.92±25.13	76.29±16.93	<0.001

In the present study the mean serum glucose value improved from 37.05±20.22 mg/dl at admission to 50.83±11.83 mg/dl at discharge in birth asphyxiated

babies and the difference was statistically significant. Similarly the serum glucose values improved from 46.92±25.13 mg/dl at admission to 76.29±16.93 mg/dl at discharge in septicemic neonates who were treated with antibiotics and supportive measures. The difference was statistically highly significant.

SERUM CALCIUM

In the present study, the overall mean serum calcium level at admission in the critically ill neonates irrespective of birth weight, sex, gestational age and clinical diagnosis was 7.720±1.699 mg/dl.

In contrast to this, Sharma et al (1993) in her study of serum calcium level in healthy neonates reported a mean value of 12.31±3.60 mg/dl at birth.

Vegad et al (1975) reported a mean value of 10.00±2.8 mg/dl in healthy neonates at birth. Similarly Acharya and Payne (1965) reported slightly lower mean serum calcium value in healthy neonates i.e. 9.4 mg/dl. Stoliar et al (1971) found a mean serum calcium level of 9.20±0.36 mg/dl in his control group of healthy neonates at admission.

Thus in the present study of serum calcium level in critically sick neonates, the levels are less than those reported by various workers in healthy neonates Decreased serum calcium levels in critically sick patients have been observed by many workers viz. Zaloga et al (1987), Sanchez et al (1987) and Rivero et al (1988).

The lowered serum calcium values in critically sick patients is due to increased serum calcitonin levels as reported by Zaloga et al (1987) in adults, Sanchez et al (1989) in children and Venkataraman et al (1987) in neonates. Calcitonin results in lowering of serum calcium through its antagonism of the calcium mobilizing effect of parathyroid hormone on bone and its calciuretic effect in the kidney.

a. Relation with Birth asphyxia

In the present study mean serum calcium value in birth asphyxiated babies, irrespective of sex and gestational age at admission was 7.47 ± 1.97 mg/dl.

Tsang et al (1974) in a similar study reported a mean serum calcium value of 7.51 ± 0.25 mg/dl in asphyxiated babies at 24 hours of age, compared with 8.13 ± 0.23 mg/dl in control infants ($p < 0.025$).

Similarly Stoliar et al (1971) found lower serum calcium levels in birth asphyxiated babies with Apgar scores below three.

The lowered serum calcium in birth asphyxiated babies is due to elevated glucagon concentration (Johnston et al, 1973) which is a calcitonin secretagogue (Swaminathan, 1973). However, Venkataraman et al (1987) found significant inverse relationship of serum calcium to serum calcitonin, but not glucagon concentration in birth asphyxiated babies.

Tsang et al (1973) attributed neonatal hypocalcemia in birth asphyxiated babies to hyperphosphatemia which results from excessive endogenous breakdown of glycogen and tissue proteins (Mc Cance et al, 1954).

In the present study lower serum calcium levels could also be attributed to refusal of feeds or inability to accept feeds by birth anoxic babies coupled with delayed beginning of feeds by mothers due to cultural taboos. Sanchez et al (1989) has also stressed altered dietary intakes in critically ill children as a possible cause of hypocalcemia in them.

b. Relation with Septicemia

In the present study, the mean serum calcium at admission in critically sick neonates irrespective of sex and gestational age, was 7.75 ± 1.53 mg/dl.

Reference ranges of serum calcium in septicemic neonates are lacking.

Zaloga et al (1987) reported lower serum calcium values in septicemic adults, and attributed it to acquired parathyroid gland insufficiency, vitamin D deficiency and acquired calcitriol resistance.

Altered nutrient intake could also be responsible for lowered serum calcium observed in septicemic neonates.

c. Correlation of serum calcium with gestational age in sick neonates

1. The serum calcium at admission in septicemic preterm babies was 7.22 ±1.30 mg/dl as against 7.93±1.55 mg/dl in septicemic term babies. Although the observed mean serum calcium in preterm babies was low as compared to full term babies, the difference was not statistically significant (p >0.5).
2. In the birth anoxic group , serum calcium value at admission in preterm babies was 7.05±1.77 mg/dl which was lower than seen in term babies (7.75±2.07 mg/dl). The difference however, was not statistically significant.

The mean calcium value reported by Vegad et al (1975) in otherwise healthy preterm babies was lower (9.01±3.34 mg/dl) than seen in full term babies(10.0±2.81 mg/dl)a finding which is similar to the present study.

Sharma et al (1993) also reported lower serum calcium values in otherwise healthy preterm babies (10.8±4.33 mg/dl) as compared to full term babies(12.44 ±3.81 mg/dl) but the difference was not statistically significant.

Thus, in conclusion, one could say that lower serum calcium values are present in premature babies possibly as a result of functionally immature and suppressed parathyroids which are unable to maintain normocalcemia (Tsang et al, 1973). The condition is

further aggravated by stressful situation like asphyxia or septicemia.

CHANGES IN SERUM CALCIUM FROM ADMISSION TO DISCHARGE

TABLE XXX : Showing significance of difference between serum calcium values at admiission and at discharge in birth asphyxiated and septicemic babies. (mg/dl).

Sl. No.	Diagnosis	At admission Mean ± S.D.	At discharge Mean±S.D.	p value
1.	Birth anoxia	7.46±1.97	9.00±1.36	<0.02
2.	Septicemia	7.75±1.52	9.30±0.99	<0.001

In the present study the mean serum calcium improved from 7.46±1.97 mg/dl at admission to 9.0±1.36 mg/dl at discharge in birth asphyxiated babies and the difference was statistically significant.

Similarly, the serum calcium value improved from 7.75±1.52 mg/dl at admission to 9.30±0.99 mg/dl at discharge in septicemic babies and the difference was statistically significant.

SERUM UREA NITROGEN AND SERUM UREA

In the present study overall mean serumurea value in the critically ill neonates at admission, irrespective of birth weight, sex, gestational age and clinical diagnosis was 63.58±46.71 mg/dl. Reference ranges of serum urea in ciritically ill neonates are lacking.

In contrast to this Sharma et al (1993), in her study of serum urea values in healthy neonates reported a mean value of 23.08±11.80 mg/dl. Similarly Acharya and Payne (1965) reported the mean level of urea in cord blood as being 29.37±7.3 mg/dl, which is lower than that found in the present study. The higher mean serum urea levels could be due to the failure of immature kidneys of neonates to adapt to stressful shock conditions, leading to renal dysfunction.

Relation with birth asphyxia

The serum urea value in birth asphyxiated babies irrespective of gestational age at admission was 84.63±51.24 mg/dl.

Reference ranges of serum urea in birth asphyxiated babies are lacking. The higher values in birth asphyxiated babies could be due to the anoxic renal injury leading to medullary and/or cortical necrosis thereby compromising the renal function.

Relation with Septicemia

In present study, serum urea value in septicemic neonates at admission, irrespective of gestational age and sex was 54.76±41.73 mg/dl. Reference ranges of serum urea in septicemic neonates are lacking. The higher serum urea value in septicemic neonates could also occur as a result of ischemic renal injury consequent upon septicemic shock (Saili et al, 1991).

Correlation of serum urea with gestational age in sick neonates.

1. The serum urea at admission in septicemic preterm babies was 48.4±24.46 mg/dl as against 56.96±46.01 mg/dl in full term babies. The difference, however, was not statistically significant (p >0.5).
2. In the birth anoxic group serum urea at admission in preterm babies was 85.15±46.99 mg/dl as against 78.94±53.55 mg/dl in full term babies. The difference was not statistically significant(p >0.5).

Vegad et al (1974) did not find much difference in serum urea values between the preterm and full term healthy neonates. The authors reported a mean serum urea value of 23.52±4.78 mg/dl and 23.20±4.56 mg/dl in preterm and full term babies respectively. Similarly Sharma et al (1993) also observed that the difference in serum urea level between preterm and full term healthy babies was not statistically significant.

CHANGES IN SERUM UREA FROM ADMISSION TO DISCHARGE

TABLE XXXI : Showing the significance of difference between serum urea values at admission and at discharge in birth asphyxiated and septicemic babies.(mg/dl).

Sl. No.	Diagnosis	Admission Mean ± SD	Discharge Mean±S.D.	p value
1.	Birth anoxia	84.63±51.24	33.68±38.99	<0.001
2.	Septicemia	54.77±41.73	25.70±18.83	<0.02

In the present study, mean serum urea value in birth anoxic babies decreased from 84.63±51.24 mg/dl at admission to 33.68±38.99 mg/dl at discharge. Similarly the mean serum urea value in septicemic neonates decreased from 54.77±4.73 mg/dl at admission to 25.7±18.83 mg/dl at discharge. This indicated a high degree of reversibility in renal function consequent to improvement of clinical status of the neonate.

SERUM CREATININE

In the present study, the overall mean serum creatinine value at admission in the critically ill neonates, irrespective of birth weight, sex, gestational age and clinical diagnosis was 1.69±0.89 mg/dl. Reference ranges of serum creatinine are lacking in critically ill neonates.

In contrast to this, Sharma et al (1993), in her study of serum creatinine values in healthy neonates reported a mean value of 1.6±0.35 mg/dl.

Thus, in the present study the mean serum creatinine levels are not different from those observed by Sharma et al (1993).

Relation with birth Asphyxia

The serum creatinine value in birth asphyxiated babies, irrespective of gestational age at admission was 2.07±0.903 mg/dl.

Reference ranges of serum creatinine in birth asphyxiated babies are lacking. The higher serum creatinine in birth asphyxiated babies is due to extreme sensitivity of kidneys to oxygen deprivation. Within 24 hours of an ischemic episode cortical or medullary necrosis occurs leading to elevated levels of serum creatinine.

Relation with Septicemia

In the present study, serum creatinine value in septicemic neonates irrespective of gestational age, and sex, at admission was 1.572±0.89 mg/dl.

References ranges of serum creatinine in septicemic babies are lacking. Under normal circumstances the kidneys of a full term neonates, although not fully mature, adapt, with most of the rapidly changing functional demands of the body. However, adaptation by the kidneys may show breakdown in the event of stressful conditions like septicemia. This may lead to renal dysfunction and elevated levels of serum creatinine.

Correlation of serum creatinine with gestational age in sick neonates

1. The serum creatinine at admission in septicemic preterm babies was 1.76±0.68 mg/dl as against 1.50±0.89 mg/dl in septicemic term babies. The difference was, however, not statistically significant ($p > 0.05$).

2. In birth anoxic group, serum creatinine at admission was 2.17±0.71 mg/dl in preterm babies as compared to 1.93±1.02 mg/dl in term babies. Although the mean serum creatinine value in preterm babies was higher than that observed in term babies, yet the difference was not statistically significant.

The mean serum creatinine reported by Rudd et al (1983) in otherwise healthy premature babies of 2 days post natal age was 1.31±0.45 mg/dl at 28 weeks, 1.18±0.43 mg/dl at 29-32 weeks and 1.05±0.44 mg/dl at 33-36 weeks gestational age. In the full term babies, mean serum creatinine was 0.85±0.43 mg/dl. Authors reported an inverse relationship of serum creatinine with increasing gestational age. These values are lower than those found in the present study. Stone-street et al (1978) reported mean serum creatinine value of 1.3±0.07 mg/dl in the first ten day of life in low birth weight babies, all of whom were premature (mean gestational age 31 weeks). Sharma et al (1993) reported the following cord blood creatinine values - 1.87±0.21, 1.58±0.37 and 1.25±0.25 mg/dl in otherwise healthy preterm, full term and post term babies respectively. Likewise Sharma et al (1993) reported higher creatinine levels in preterm as compared to term healthy babies.

The relative high levels of serum creatinine at birth are maternal in origin. Contributing to these higher levels are increased tissue destruction and reduced

glomerular filtration rate in the neonates. The higher serum creatinine value in preterm babies as compared to term babies is due to their immature renal function.

CHANGES IN SERUM CREATININE FROM ADMISSION TO DISCHARGE

TABLE XXXII: Showing the statistical significance of the difference between serum creatinine values at admission and at discharge in birth asphyxiated and septicemic babies. (mg/dl).

Sl. No.	Diagnosis	Admission Mean ±S.D.	Discharge Mean±S.D.	p value
1.	Birth anoxia	2.07±0.90	0.98±0.66	<0.001
2.	Septicemia	1.57±0.89	0.82±0.39	<0.001

In the present study mean serum creatinine values in birth asphyxiated babies decreased from 107±0.90 mg/dl at admission to 0.98±0.66 mg/dl at discharge. This could be attributed to early recognition and aggressive treatment of renal failure. The decrease in serum creatinine values of babies at discharge could be also attributed to functional improvement of glomerular filtration due to increasing post natal maturity (Rudd et al, 1983). The mean serum creatinine value in septicemic babies at admission in the present study was 1.57±0.89 mg/dl which decreased to 0.82±0.39 mg/dl at discharge. Saili et al (1991) observed that all septicemic neonates who went into shock developed acute renal failure. They concluded that sepsis caused renal [illegible] anoxia due to initial episode of shock which triggered renal failure.

SERUM BILIRUBIN

In the present study, overall mean serum bilirubin value in the critically ill neonates at admission irrespective of birth weight, sex, gestational age and clinical diagnosis was 6.35±5.14 mg/dl.

Reference ranges of serum bilirubin in critically ill neonates are lacking.

To overall mean value of serum bilirubin irrespective of birth weight, gestational age and sex, as reported by Sharma et al (1993) in the cord blood of healthy neonates was 0.46±0.23 mg/dl.

The higher mean serum bilirubin value in the present study did not reflect the effect of sickness alone on the liver function, since most of the babies were admitted in their first week of post natal life, which is also the period of physiological jaundice.

Relation with birth asphyxia

The serum bilirubin value in birth asphyxiated babies, irrespective of gestational age at admission was 7.36±5.68 mg/dl.

Saili et al (1990) in his study of liver dysfunction in severe birth asphyxia, observed mean serum bilirubin value of 4.78±6.62 mg/dl at 48-72 hours of post natal age. The mean value in the control group was 4.50±6.12 mg/dl. The higher serum bilirubin value in the present study could be due to inclusion of neonates older than 2-3 days,,when raised bilirubin levels are contributed

by the presence of physiological jaundice which is usually at its peak.

Relation with septicemia

In the present study, serum bilirubin in the septicemic neonates at admission, irrespective of gestational age and sex was 5.95±4.87 mg/dl. Reference ranges of serum bilirubin in septicemic neonates are lacking. Jaundice in septicemia is due to increased haemolysis of red blood cells (Dunham, 1933, Silverman et al, 1949). Sas-Kortsak (1956), Bernstein et al (1962) and other workers have, however, reported regurgitative jaundice in septicemic newborns, the cause of which remains poorly understood.

Correlation of serum bilirubin with the gestational age in sick neonates

1. The serum bilirubin at admission in septicemic babies was 6.61±4.14 mg/dl as against 5.73±5.08 mg/dl in full term babies. The difference was not statistically significant (p >0.6).

2. In the birth anoxic group, serum bilirubin at admission in preterm babies was 7.71±4.92 mg/dl as against 6.65±6.27 mg/dl in full term babies. The difference was, however, not statistically significant (p >0.6).

CHANGES IN SERUM BILIRUBIN FROM ADMISSION TO DISCHARGE

TABLE XXXIII : Showing the statistical significance of difference between serum bilirubin values at admission and at discharge in birth asphyxiated and septicemic babies (mg/dl).

Sl. No.	Diagnosis	Admission Mean±S.D.	Discharge Mean±S.D.	p value
1.	Birth anoxia	7.36±5.68	3.84±1.83	<0.05
2.	Septicemia	5.95±4.87	2.06±1.69	<0.001

In the present study, the mean serum bilirubin value in birth anoxic babies decreased from 7.36±5.68 mg/dl at admission to 3.84±1.83 mg/dl at discharge. Similarly, the mean serum bilirubin value in septicemic neonates decreased from 5.95±4.87 at admission to 2.06±1.69 mg/dl at discharge.

FREQUENCY DISTRIBUTION OF VARIOUS BIOCHEMICAL VALUES IN SICK NEWBORNS.

It shows the distribution of levels of serum glucose, calcium, urea, creatinine and bilirubin in the study group (Graph 1 to 5) at admission and at discharge.

The frequency distribution curve of serum sugar at admission shows two peaks.

The first peak is represented by hypoglycemic sick babies whereas the second peak accounts for the normoglycemic sick babies.

The graph at discharge of the baby shows more uniform distribution of values with a shift towards the right, indicating improved glucose levels.

The frequency distribution curve of serum calcium shows relatively lower values at admission. The shift of the curve to right side shows improved serum calcium levels at discharge.

The values of serum urea, creatinine and bilirubin show wide dispersion (vide graph No. 3, 4 & 5) at admission. However, at discharge, the curves have shifted to left with most of the values being towards the lower side.

FREQUENCY DISTRIBUTION CURVE OF SERUM GLUCOSE IN SICK NEONATES.

ADMISSION → x x x

DISCHARGE → ●—●—●

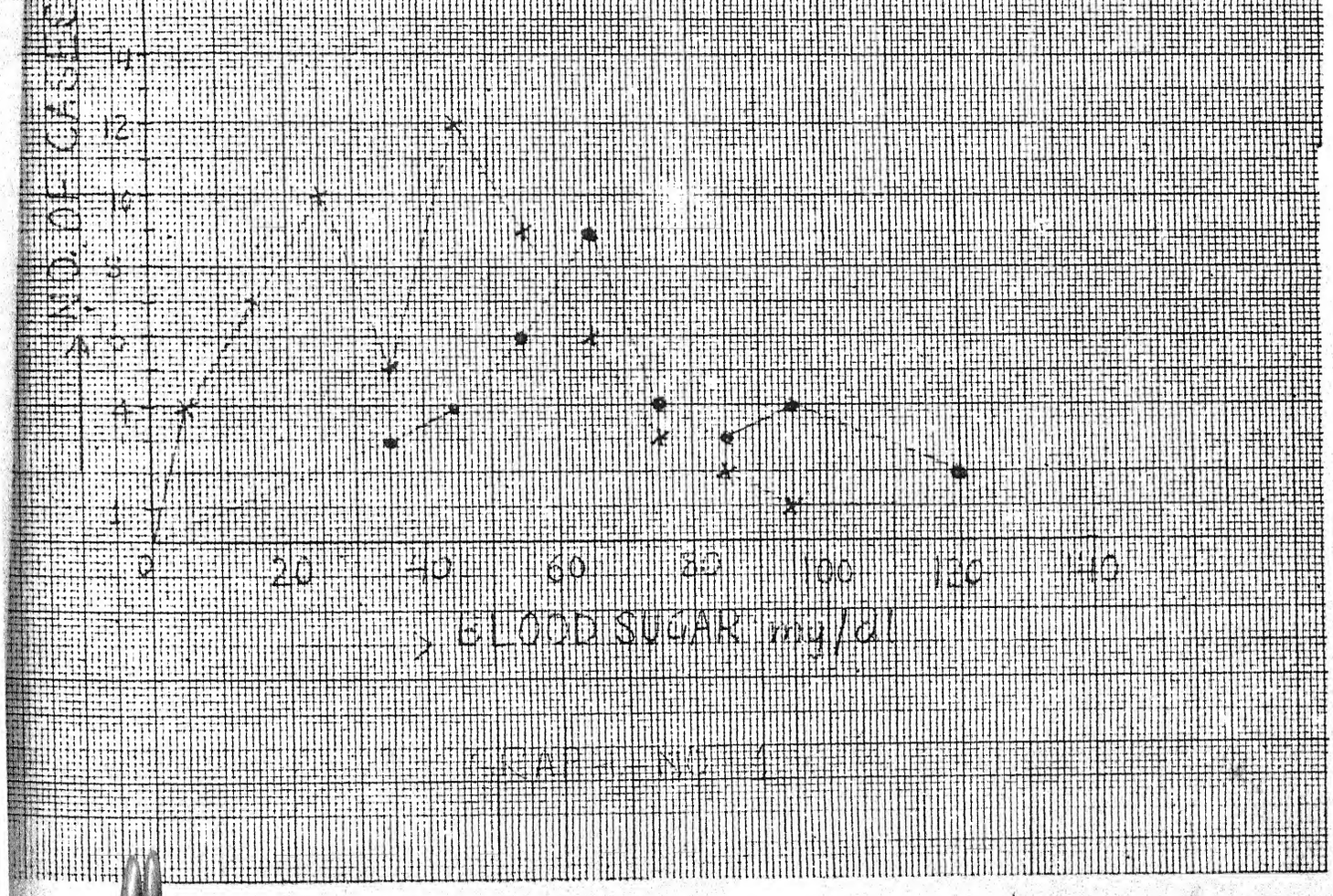
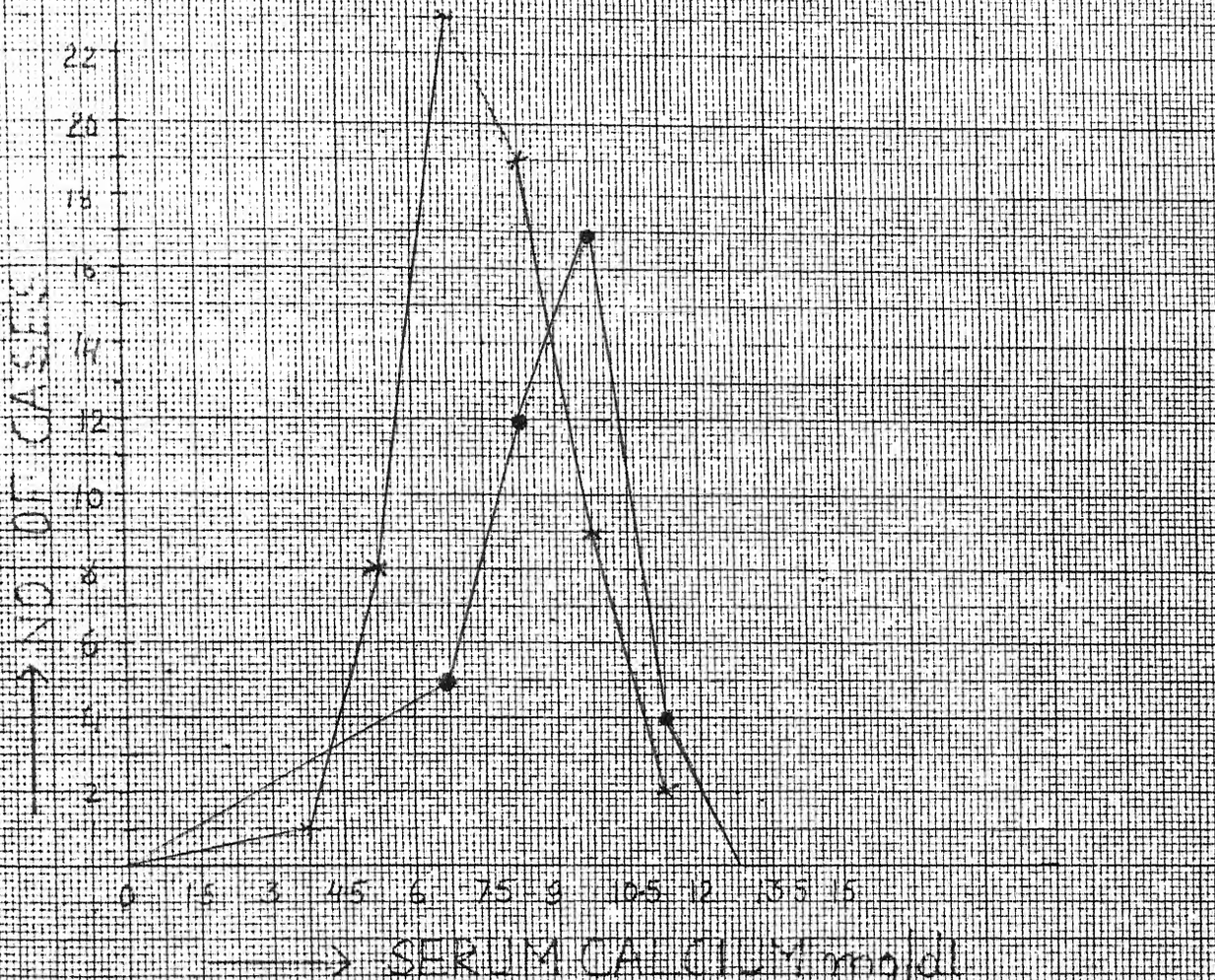


FIG. NO. 1

FREQUENCY DISTRIBUTION CURVE OF SERUM CALCIUM IN SICK NEONATES

ADMISSION → × × ×

DISCHARGE → ● ● ●

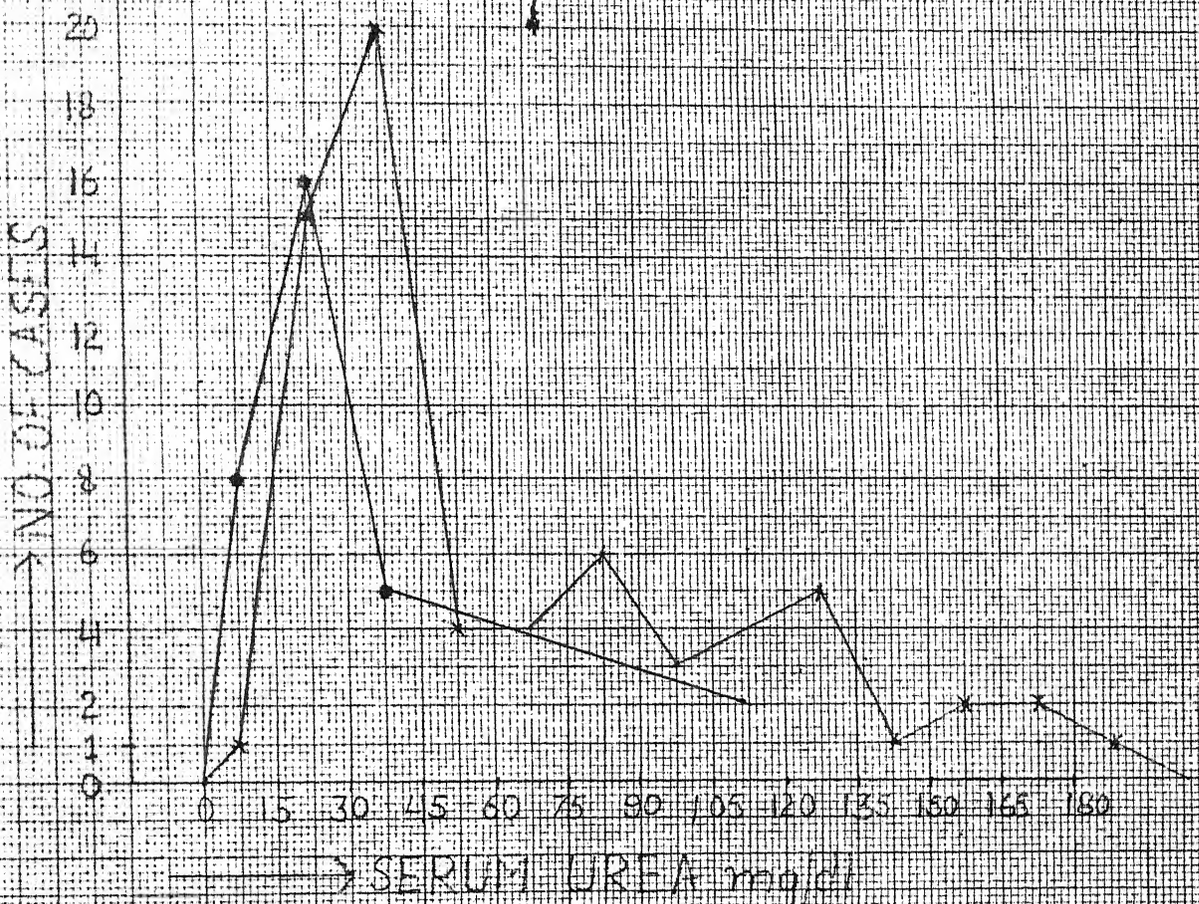


GRAPH NO. 2

FREQUENCY DISTRIBUTION CURVE OF SERUM UREA IN SICK NEONATES

ADMISSION → × × ×

DISCHARGE → ● ● ●

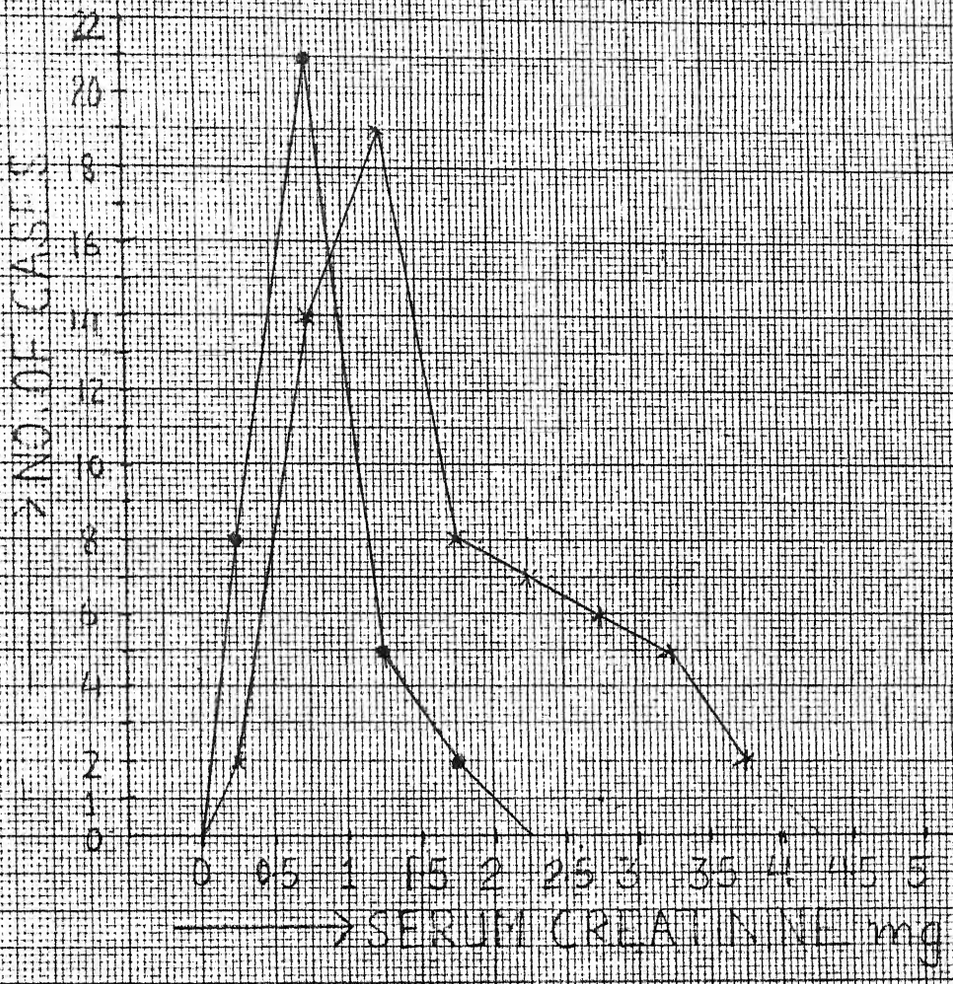


GRAPH NO-3

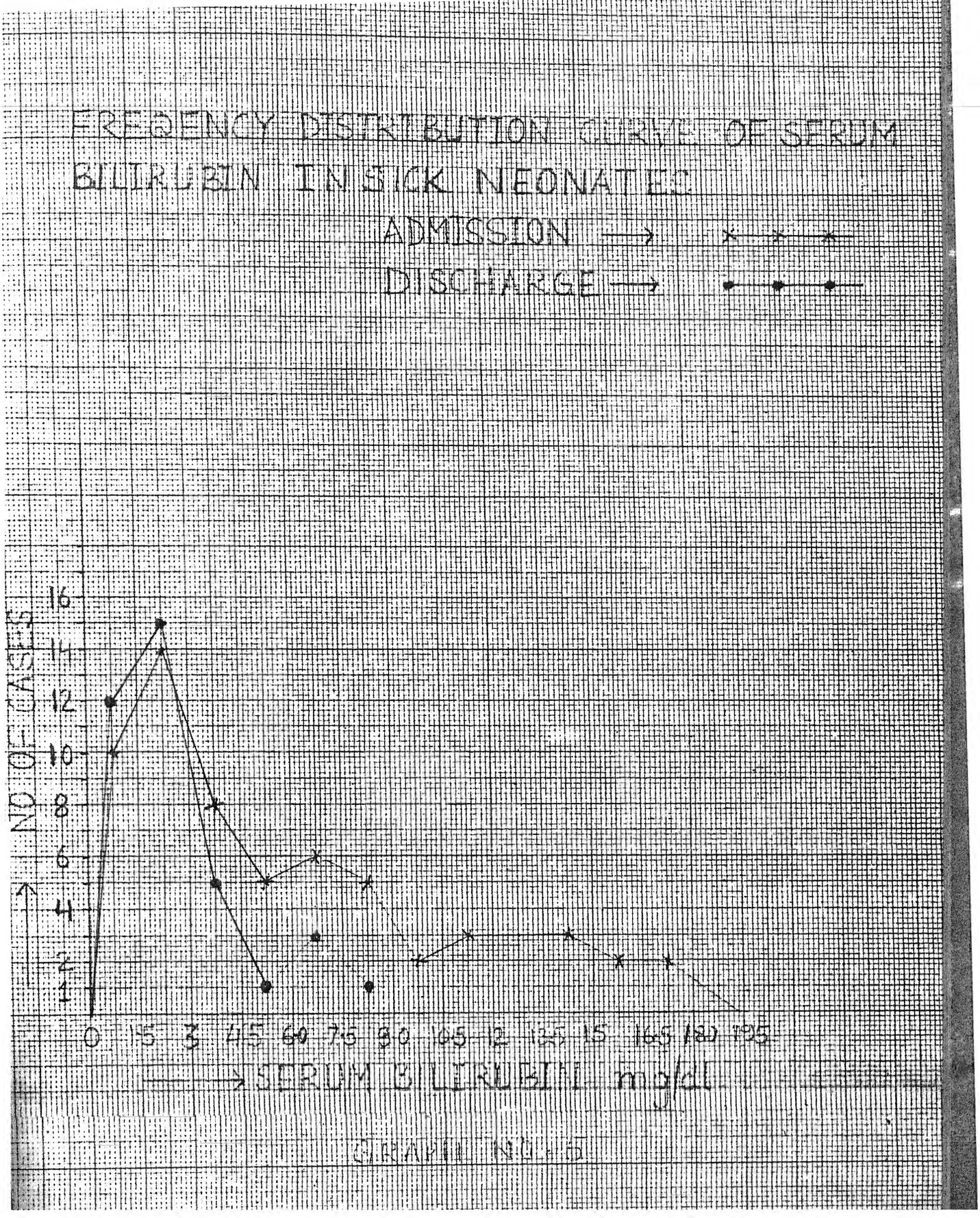
FREQUENCY DISTRIBUTION CURVE OF SERUM CREATININE IN SICK NEONATES

ADMISSION → × — × — ×

DISCHARGE → ● — ● — ●



GRAPH NO 14


FREQENCY DISTRIBUTION CURVE OF SERUM
BILIRUBIN IN SICK NEONATES
ADMISSION →
DISCHARGE →
NO OF CASES
16
14
12
10
8
6
4
2
0
1·5
3
4·5
6·0
7·5
9·0
10·5
12
13·5
15
16·5
18·0
19·5
→ SERUM BILIRUBIN mg/dl
GRAPH NO. 5

SUMMARY AND CONCLUSION

The present work was carried out to study the serum levels of glucose, urea, creatinine, calcium and bilirubin in critically sick neonates at the time of admission. Moreover, the subsequent change in these variables until the time of discharge was observed. The study was conducted at M.L.B. Medical College, Jhansi in the department of Pediatrics in collaboration with the departments of Obstetrics and Gynaecology. The estimation of biochemical values was done in the department of Biochemistry.

At admission, weight and sex of the baby was recorded and a thorough clinical examination of the baby was carried out. The gestational age was calculated by counting the number of weeks from the first day of last menstrual period until the date of birth of the baby.

The first blood sample for biochemical investigations was drawn at admission from a peripheral vein. Another sample was withdrawn at the time of discharge when the baby was clinically cured.

Critically sick neonates were categorised into three broad groups according to the clinical diagnosis viz. birth asphyxiated babies, septicemic babies and miscellaneous group. The last group comprised of those cases who did not come within the category of first two clinical diagnoses. It included two cases of respiratory

distress syndrome, one of congenital malarial and one case of epidermolysis bullosa.

In all, sixty four babies (less than 28 days of post natal age) were included in the study. There were 21 cases of birth asphyxia (32.81%) and 39(60.94%) cases of septicemia. There were 4(6.25%) babies in the miscellaneous group.

On the basis of gestational age, septicemic and birth asphyxiated babies were again subdivided into preterm, full term and post term babies. The study included 45 (70.31%) male and 17(29.31%) female babies.

BIRTH ASPHYXIATED BABIES

This group of neonates comprised of 21 babies : 10(47.62%) female and eleven(52.38%) male. There were 9(42.86%) preterm babies and 11(52.38%) full term babies. Besides these one baby was a post term.

Out of twenty one birth asphyxiated babies, three left the study during the course of treatment and among the remaining eighteen, seven (38.89%) died and eleven (61.11%) improved.

1. Biochemical values at admission in birth asphyxiated babies

In the present study, mean values of serum glucose, calcium, urea, urea nitrogen, creatinine and bilirubin at admission, irrespective of birth weight, and sex were observed as follows :

a.	Serum glucose	: 37.05±20.22 mg/dl
b.	Serum calcium	: 7.46±1.97 mg/dl
c.	Serum urea	: 84.63±51.24 mg/dl.
d.	Serum urea nitrogen	: 39.54±23.93 mg/dl.
e.	Serum creatinine	: 2.07±0.90 mg/dl.
f.	Serum bilirubin	: 7.36±5.68 mg/dl.

2. Biochemical values at discharge in birth asphyxiated babies

In the present study, mean values of serum glucose, calcium, urea, urea nitrogen, creatinine and bilirubin at the time of discharge irrespective of birth weight, sex and gestational age were as follows :

a.	Serum glucose	: 50.83±11.83 mg/dl
b.	Serum calcium	: 9.0±1.36 mg/dl
c.	Serum urea	: 33.68±38.99 mg/dl.
d.	Serum urea nitrogen	: 16.48±18.01 mg/dl
e.	Serum creatinine	: 0.98±0.66 mg/dl.
f.	Serum bilirubin	: 3.84±1.83 mg/dl.

A statistically significant change was observed in all the biochemical parameters in critically sick neonates from admission to the time of discharge, when they were clinically cured.

3. Variation in biochemical values according to gestational age* at the time of admission.

Sl. No.	Biochemical values	Preterm (mg/dl)	Full term (mg/dl)
1.	Serum glucose	29.50±19.06	44.19±19.37
2.	Serum calcium	7.05±1.77	7.75±2.07
3.	Serum urea	85.15±46.99	78.94±53.55
4.	Serum urea nitrogen	39.77±21.93	36.88±25.02
5.	Serum creatinine	2.17±0.71	1.93±1.02
6.	Serum bilirubin	7.71±4.92	6.65±6.27

(*There was only one neonate in post term group)

At the time of admission, maturity status had no significant effect on any of the biochemical values in the critically sick neonates.

SEPTICEMIC BABIES

This group comprised of 39 babies : 31(79.49%) male and 8(20.51%) female.

The group included 10(25.64%) preterm and 29(74.36%) full term babies.

In this group, four babies dropped out from the study. Out of the remaining 35 neonates, 11(31.43%) died and 24 (68.57%) improved.

1. Biochemical values at admission in septicemic babies.

In the present study, mean values of serum glucose, calcium, urea, urea nitrogen, creatinine and bilirubin at admission irrespective of birth weight, sex and gestational age were as follows :

a.	Serum glucose	: 46.92±25.13 mg/dl
b.	Serum calcium	: 7.75±1.52 mg/dl
c.	Serum urea	: 54.76±41.73 mg/dl
d.	Serum urea nitrogen	: 25.59±19.50 mg/dl
e.	Serum creatinine	: 1.57±0.89 mg/dl
f.	Serum bilirubin	: 5.95±4.87 mg/dl.

2. Biochemical values at discharge in septicemic babies

In the present study the mean values of serum glucose, calcium, urea, urea nitrogen, creatinine and bilirubin at the time of discharge irrespective of birth weight, sex and gestational age were as follows :-

a.	Serum glucose	: 76.29±16.93 mg/dl.
b.	Serum calcium	: 9.3±0.99 mg/dl
c.	Serum urea	: 25.7±18.83 mg/dl
d.	Serum urea nitrogen	: 11.53±8.86 mg/dl
e.	Serum creatinine	: 0.82±0.39 mg/dl.
f.	Serum bilirubin	: 2.06±1.69 mg/dl.

A statistically significant change was observed in all the biochemical parameters in critically sick neonates from admission to the time of discharge, when they were clinically cured.

3. Relation of biochemical values with gestational age* at admission

The variation in biochemical values according to the gestational age observed at the time of admission was as follows :

Sl. No.	Biochemical values	Preterm (mg/dl)	Full term (mg/dl)
1.	Serum glucose	34.95±20.09	51.30±25.25
2.	Serum calcium	7.22±1.30	7.93±1.55
3.	Serum urea	48.40±24.46	56.96±46.01
4.	Serum urea nitrogen	22.62±11.42	26.61±21.50
5.	Serum creatinine	1.76±0.67	1.50±0.89
6.	Serum bilirubin	6.61±4.41	5.73±5.08

(*There was no baby in post term group)

There was no significant variation observed in any of the biochemical values according to the maturity status in the septicemic babies.

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B I B L I O G R A P H Y

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A P P E N D I X

APPENDIX

STUDY OF BIOCHEMICAL VALUES IN SICK NEWBORN BABIES

Department of Pediatrics, Neonatology Unit

Investigator : Dr. Dinesh Kumar,

Guide : Dr. Ramesh Kumar,
Professor and Head,
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Case No. ____

MRD No. Date :

Name Sex :

Date of Birth :

Father's Name: Age :

Father's Name: Age :

Caste :

Socio-economic status:

Address :

Diagnosis :

HISTORY

I. CHIEF COMPLAINTS

a. Refusal of feeds b. Convulsions

c. Jitteriness d. Tremors

e. Apnea f. Cianosis

g. Apathy/irritability h. Hypotonia

i. Delayed cry/weak cry/excessive crying

j. Respiratory difficulty/distress

k. Discharge from umbilical stump

l. Not passed urine m. Diarrhoea/dehydration

n. Distension of abdomen o. Fever

p. Jaundice q. Rashes

r. Others.

II. HISTORY OF PRESENT ILLNESS

III. BRIEF OBSTETRICAL HISTORY OF MOTHERS

Gravida Parity Abortion

- Last menstrual period :
- Gestational Age :
  a. According to L.M.P. :
  b. Using Dubonitz Criteria:
- Previous evidence of bad obstetrical history (Specify).
- Others :

IV. ANTENATAL HISTORY

Fever

Swelling over limbs/ pre-eclampsia

Maternal Smoking

Antepartum haemorrhage

Immunized/unimmunized

Leaking P.V.
  a. More than 12 hours.
  b. Less than 12 hours.

Rashes

Convulsions/eclampsia

Drug intake

Exposure to Radiation

Whether received supplementation of Iron/Vit./ minerals

Chronic diseases with special reference to :

Diabetes mellitus Hypertension

Thyrotoxicosis Others

V. NATAL HISTORY

a. Presentation
b. Duration of labour
c. Evidences of Fetal distress.
d. Time of rupture of fetal membranes
e. Mode of delivery :
   - Normal vaginal.
   - Forceps
   - Caesarean
g. Any feature of Birth asphyxia/Apgar score
h. Maternal medication :
   - Syntocinon drip/other betamimetic agents
   - Analgesia

- Anaesthesia - general/spinal/local
- Other drugs - Theophylline
- Corticosteroids

i. Resuscitative methods/procedures employed (Details thereof).

j. Others :

VI. DIETARY AND PERSONAL HISTORY OF MOTHER

Vegetarian / Non-vegetarian

Average intake : Calories

: Proteins

VII. SMOKING HISTORY

VIII. FAMILY HISTORY

IX. EXAMINATION OF MOTHER

General examination
General appearance
Nutrition
Built
Hydration
Pallor
Icterus
Oedema

Clubbing
Lymphadenopathy
Pulse rate
Respiratory rate
Temperature
Blood pressure
Weight
Height

SYSTEMIC EXAMINATION

Cardiovascular System

Respiratory System

Gastrointestinal System

Central Nervous System

EXAMINATION OF NEONATE

I. GENERAL APPEARANCE

Activity
Colour
Cry
Posture

II. ANTHROPOMETRIC EXAMINATION

Weight — Head circumference :

Length — Chest circumference:

III. GENERAL EXAMINATION

Heart rate	Respiratory rate
Temperature	Purpuric rashes
Edema	Icterus
Heal - Anterior Fontanelle	Eyes
Scalp - Caput	Oral cavity
Cephalhaematoma	Neck and Trunk
Others	Umbilicus
Ganatalia	Extremities
Any other congenital anomaly	Others.

IV. SYSTEMIC EXAMINATION

Cardiovascular System

Respiratory System

Gastrointestinal System

Neurological Examination

a. Neurological reflexes : Rooting reflex
: Sucking reflex
: Moro reflex
: Pupillary reflex
: Deep tendon jerks

b. Tone : Anterior Fontanelle

INVESTIGATIONS

Sl. No.	Date	Blood sample	Urea (mg%)	Creatinine (mg%)	Glucose (mg%)	Calcium (mg%)	Bilirubin (mg%)
1.		On Admission					
		Umbilical vein					
		Peripheral vein					
2.		On Clinical cure					
		Umbilical vein					
		Peripheral vein					